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L1             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  US2004-518503/APPS


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L1   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2004:2882  HCAPLUS  Full-text
DOCUMENT NUMBER:          140:77154
TITLE:                    Preparation of thiazoles as phosphodiesterase IV
                          inhibitors for the treatment of osteoporosis, tumors
                          and cachexia
INVENTOR(S):              Egggenweiler, Hans-Michael; Wolf, Michael
PATENT ASSIGNEE(S):       Merck Patent G.m.b.H., Germany
SOURCE:                   PCT Int. Appl., 125 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2004000839         A1    20031231    WO 2003-EP4434          20030428
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     DE 10227269           A1    20040108    DE 2002-10227269        20020619
     CA 2489902            A1    20031231    CA 2003-2489902         20030428
     AU 2003232215         A1    20040106    AU 2003-232215          20030428
     BR 2003011879         A     20050315    BR 2003-11879           20030428
     EP 1513837            A1    20050316    EP 2003-760583          20030428
     EP 1513837            B1    20060830
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     CN 1662529            A     20050831    CN 2003-814060          20030428
     JP 2005530825         T     20051013    JP 2004-514623          20030428
     AT 338041             T     20060915    AT 2003-760583          20030428
     US 2005222160         A1    20051006    US 2004-518503          20041220 <--
PRIORITY APPLN. INFO.:                        DE 2002-10227269    A   20020619
                                              WO 2003-EP4434      W   20030428

OTHER SOURCE(S):          MARPAT 140:77154
ED   Entered STN:  02 Jan 2004
AB   Title compds. I [R1, R2 = H, OH, OR8, etc.; R8 = A, cycloalkyl, alkenyl, etc.;
     R3 = H, A"R7, COA"R7, etc.; A = alkyl, alkenyl; R7 = H, CO2H, CONH2, etc.; A"
     = alkylene, alkenylene, cycloalkylene, etc.; V, W = O, OH with the proviso
     that if V = O, then W = H, H; B = (un)substituted aromatic isocyclic,
     heterocyclic e.g., pyridyl, pyridyl-N- oxide, thienyl, etc.; X = N, CR3] their
     pharmaceutically acceptable salts and formulations were prepared  For example,
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coupling of acid chloride II, e.g., prepared from 4-methyl-2-pyridin-2-ylthiazole-5-carboxylic acid Me ester in 3-steps, and 3-(3-cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazine afforded claimed thiazole III. Compds. I are claimed useful as phosphodiesterase IV inhibitors (no data provided) for the treatment of osteoporosis, tumors, cachexia, etc.

IC ICM C07D417-14
ICS C07D417-06; A61K031-50; A61P011-06; A61P019-02; A61P019-10; A61P029-00; A61P035-00

CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

ST osteoporosis prepn phosphodiesterase thiazole inhibition; tumor prepn phosphodiesterase thiazole inhibition; cachexia prepn phosphodiesterase thiazole inhibition

IT Inflammation
(Crohn's disease; preparation of thiazoles as phosphodiesterase IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

IT Intestine, disease
(Crohn's; preparation of thiazoles as phosphodiesterase IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

IT Dermatitis
(atopic; preparation of thiazoles as phosphodiesterase IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

IT Bronchi, disease
Inflammation
(chronic bronchitis; preparation of thiazoles as phosphodiesterase IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

IT Neoplasm
(metastasis; preparation of thiazoles as phosphodiesterase IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

IT AIDS (disease)
Allergy
Allergy inhibitors
Anti-AIDS agents
Anti-inflammatory agents
Antiarteriosclerotics
Antiasthmatics
Antidiabetic agents
Antirheumatic agents
Antitumor agents
Arteriosclerosis
Asthma
Autoimmune disease
Cachexia
Cardiovascular agents
Diabetes mellitus
Heart, disease
Human
Inflammation
Multiple sclerosis
Neoplasm
Osteoporosis
Psoriasis
Rheumatoid arthritis
Sepsis
Skin, disease
(preparation of thiazoles as phosphodiesterase IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

IT Inflammation

Intestine, disease
(ulcerative colitis; preparation of thiazoles as phosphodiesterase IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

IT 640743-35-7P 640743-36-8P 640743-37-9P 640743-38-0P, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyridin-3-ylthiazol-5-yl)methanone 640743-39-1P, 1-[3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyridin-3-ylthiazol-5-yl)methanone 640743-40-4P, 1-[3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyridin-3-ylthiazol-5-yl)methanone 640743-41-5P, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyridin-2-ylthiazol-5-yl)methanone 640743-42-6P, 1-[3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyridin-2-ylthiazol-5-yl)methanone 640743-43-7P, 1-[3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyridin-2-ylthiazol-5-yl)methanone 640743-44-8P, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyrazin-2-ylthiazol-5-yl)methanone 640743-45-9P, 1-[3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyrazin-2-ylthiazol-5-yl)methanone 640743-46-0P, 1-[3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyrazin-2-ylthiazol-5-yl)methanone 640743-47-1P, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-thiophen-2-ylthiazol-5-yl)methanone 640743-48-2P, 1-[3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-thiophen-2-ylthiazol-5-yl)methanone 640743-49-3P, 1-[3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-thiophen-2-ylthiazol-5-yl)methanone 640743-50-6P, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-phenylthiazol-5-yl)methanone 640743-51-7P, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-[4-methyl-2-(4-methoxyphenyl)thiazol-5-yl]methanone 640743-52-8P, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-[4-methyl-2-(4-aminophenyl)thiazol-5-yl]methanone 640743-53-9P 640743-54-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of thiazoles as phosphodiesterase IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

IT 640743-56-2P 640743-57-3P 640743-58-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of thiazoles as phosphodiesterase IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

IT 9036-21-9, Phosphodiesterase IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of thiazoles as phosphodiesterase IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

IT 109-77-3, Propanedinitrile 937-14-4 257876-11-2 438627-45-3, 3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazine 640743-55-1, 4-Methyl-2-pyridin-2-ylthiazole-5-carboxylic acid methyl ester 640743-59-5, 3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazine 640743-60-8, 3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazine 640743-61-9 640743-62-0 640743-63-1 640743-64-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of thiazoles as phosphodiesterase IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L2             1 SEA FILE=WPIX ABB=ON  PLU=ON  US2004-518503/APPS


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L2   ANSWER 1 OF 1  WPIX COPYRIGHT 2006       THE THOMSON CORP on STN
ACCESSION NUMBER:     2004-099097 [10]   WPIX
DOC. NO. CPI:         C2004-040948 [10]
TITLE:                New thienyl or thiazolyl-substituted 3-phenyl-5,6-dihydro-
                      4H-pyridazines, useful as phosphodiesterase IV inhibitors
                      for treating e.g. asthma, allergy, inflammation, or
                      autoimmune or myocardial disease
DERWENT CLASS:        B02; B03; B05; C02; C03; D21
INVENTOR:             EGGENWEILER H; EGGGENWEILER H; EGGGENWEILER H M; WOLF M
PATENT ASSIGNEE:      (EGGE-I) EGGENWEILER H; (MERE-C) MERCK PATENT GMBH;
                      (WOLF-I) WOLF M
COUNTRY COUNT:        101

PATENT INFORMATION:

      PATENT NO      KIND DATE     WEEK     LA  PG          MAIN IPC
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      WO 2004000839  A1 20031231 (200410)* DE  125[0]
      DE 10227269    A1 20040108 (200412)  DE
      AU 2003232215  A1 20040106 (200447)  EN
      EP 1513837     A1 20050316 (200519)  DE
      BR 2003011879  A  20050315 (200522)  PT
      KR 2005019141  A  20050228 (200545)  KO              C07D417-14
      US 20050222160 A1 20051006 (200566)  EN
      JP 2005530825  W  20051013 (200568)  JA  73          C07D417-06
      MX 2004012428  A1 20050501 (200572)  ES
      CN 1662529     A  20050831 (200621)  ZH  [1]
      ZA 2005000484  A  20060426 (200635)  EN  130         C07D000-00
      EP 1513837     B1 20060830 (200657)  DE
      DE 50304867    G  20061012 (200670)  DE

APPLICATION DETAILS:

      PATENT NO      KIND                  APPLICATION    DATE
      ------------------------------------------------------------------
      WO 2004000839 A1                     WO 2003-EP4434 20030428
      DE 10227269 A1                       DE 2002-10227269 20020619
      AU 2003232215 A1                     AU 2003-232215 20030428
      BR 2003011879 A                      BR 2003-11879 20030428
      DE 50304867 G                        DE 2003-504867 20030428
      EP 1513837 A1                        EP 2003-760583 20030428
      EP 1513837 B1                        EP 2003-760583 20030428
      DE 50304867 G                        EP 2003-760583 20030428
      EP 1513837 A1                        WO 2003-EP4434 20030428
      US 20050222160 A1                    WO 2003-EP4434 20030428
      JP 2005530825 W                      WO 2003-EP4434 20030428
      MX 2004012428 A1                     WO 2003-EP4434 20030428
      EP 1513837 B1                        WO 2003-EP4434 20030428
      DE 50304867 G                        WO 2003-EP4434 20030428
      JP 2005530825 W                      JP 2004-514623 20030428
      MX 2004012428 A1                     MX 2004-12428 20041209
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KR 2005019141 A	KR 2004-720522 20041217
US 20050222160 A1	**US 2004-518503 20041220**
ZA 2005000484 A	ZA 2005-484 20050118
CN 1662529 A	CN 2003-814060 20030428
CN 1662529 A	WO 2003-EP4434 20030428

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 2003232215	A1	Based on	WO 2004000839	A
EP 1513837	A1	Based on	WO 2004000839	A
BR 2003011879	A	Based on	WO 2004000839	A
JP 2005530825	W	Based on	WO 2004000839	A
MX 2004012428	A1	Based on	WO 2004000839	A
EP 1513837	B1	Based on	WO 2004000839	A
DE 50304867	G	Based on	EP 1513837	A
DE 50304867	G	Based on	WO 2004000839	A

PRIORITY APPLN. INFO: DE 2002-10227269 20020619
INT. PATENT CLASSIF.:

MAIN: C07D; C07D417-06; C07D417-14

SECONDARY: A61K; A61P; A61K031-501; A61P001-00; A61P001-04; A61P001-16; A61P011-00; A61P011-02; A61P011-06; A61P011-08; A61P013-08; A61P013-12; A61P017-00; A61P017-02; A61P017-04; A61P017-06; A61P019-02; A61P019-06; A61P019-10; A61P021-04; A61P025-00; A61P025-14; A61P025-16; A61P025-24; A61P025-28; A61P027-02; A61P027-14; A61P029-00; A61P003-10; A61P031-04; A61P031-10; A61P031-16; A61P031-18; A61P031-20; A61P031-22; A61P033-02; A61P033-06; A61P035-00; A61P037-02; A61P037-06; A61P037-08; A61P043-00; A61P005-14; A61P007-00; A61P007-04; A61P007-06; A61P009-00; A61P009-10

IPC ORIGINAL: A61K0031-50 [I,A]; A61K0031-50 [I,A]; A61K0031-50 [I,C]; A61P0011-00 [I,C]; A61P0011-00 [I,C]; A61P0011-06 [I,A]; A61P0011-06 [I,A]; A61P0019-00 [I,C]; A61P0019-00 [I,C]; A61P0019-02 [I,A]; A61P0019-02 [I,A]; A61P0019-10 [I,A]; A61P0019-10 [I,A]; A61P0029-00 [I,A]; A61P0029-00 [I,A]; A61P0029-00 [I,C]; A61P0035-00 [I,A]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; C07D0417-00 [I,C]; C07D0417-00 [I,C]; C07D0417-00 [I,C]; C07D0417-06 [I,A]; C07D0417-06 [I,A]; C07D0417-14 [I,A]; C07D0417-14 [I,A]

IPC RECLASSIF.: A61K0031-501 [I,A]; A61K0031-501 [I,C]; A61P0001-00 [I,A] ; A61P0001-00 [I,C]; A61P0001-04 [I,A]; A61P0001-16 [I,A] ; A61P0011-00 [I,A]; A61P0011-00 [I,C]; A61P0011-02 [I,A] ; A61P0011-06 [I,A]; A61P0011-08 [I,A]; A61P0013-00 [I,C] ; A61P0013-08 [I,A]; A61P0013-12 [I,A]; A61P0017-00 [I,A] ; A61P0017-00 [I,C]; A61P0017-02 [I,A]; A61P0017-04 [I,A] ; A61P0017-06 [I,A]; A61P0019-00 [I,C]; A61P0019-02 [I,A] ; A61P0019-06 [I,A]; A61P0019-10 [I,A]; A61P0021-00 [I,C] ; A61P0021-04 [I,A]; A61P0025-00 [I,A]; A61P0025-00 [I,C] ; A61P0025-14 [I,A]; A61P0025-16 [I,A]; A61P0025-24 [I,A] ; A61P0025-28 [I,A]; A61P0027-00 [I,C]; A61P0027-02 [I,A] ; A61P0027-14 [I,A]; A61P0029-00 [I,A]; A61P0029-00 [I,C] ; A61P0003-00 [I,C]; A61P0003-10 [I,A]; A61P0031-00 [I,C] ; A61P0031-04 [I,A]; A61P0031-10 [I,A]; A61P0031-16 [I,A] ; A61P0031-18 [I,A]; A61P0031-20 [I,A]; A61P0031-22 [I,A] ; A61P0033-00 [I,C]; A61P0033-02 [I,A]; A61P0033-06 [I,A] ; A61P0035-00 [I,A]; A61P0035-00 [I,C]; A61P0037-00 [I,C]

; A61P0037-02 [I,A]; A61P0037-06 [I,A]; A61P0037-08 [I,A]
; A61P0043-00 [I,A]; A61P0043-00 [I,C]; A61P0005-00 [I,C]
; A61P0005-14 [I,A]; A61P0007-00 [I,A]; A61P0007-00 [I,C]
; A61P0007-04 [I,A]; A61P0007-06 [I,A]; A61P0009-00 [I,A]
; A61P0009-00 [I,C]; A61P0009-10 [I,A]; C07D0417-00 [I,C]
; C07D0417-06 [I,A]; C07D0417-14 [I,A]; A61K0031-50 [I,A]
; A61K0031-50 [I,C]

BASIC ABSTRACT:

WO 2004000839 A1 UPAB: 20060121

NOVELTY - 1-((2-(Hetero)aryl-5-thienyl or -thiazolyl)-alkyl or -carbonyl)-3-phenyl-5,6-dihydro-4H-pyridazine derivatives (I) are new.

DETAILED DESCRIPTION - Pyridazine derivatives of formula (I) and their derivatives, solvates and stereoisomers (including mixtures in all ratios) are new.

R1, R2 = H, OH, OR8, SR8, SOR8, SO2R8 or halo;

R1 + R2 = OCH2O or OCH2CH2O;

R3 = H, A2R7, COA2R7, COOA2R7, CONH2, CONHA2R7, CON(A2R7)A3R7, NH2, NHA2R7, N(A2R7)A3R7, NHCOA2R7 or NHCOOA2R7;

one of V, W' = O and the other = H2;

B = isocyclic or heterocyclic aromatic group, substituted by R4-R6;

X = N or C(R31);

R31 = R3;

R4-R6 = H, A2R7, OH, OA2R7, NO2, NH2, NHA2R7, N(A2R7)A3R7, NHCOA2R7, NHCOOA2R7, NHCONH2, NHCONHA2R7, NHCON(A2R7)A3R7, halo, COOH, COOA2R7, CONH2, CONHA2R7, CON(A2R7)A3R7, -NH-N=C(CN)-Q or lactam group of formula (a);

Q = CN, CONH2 or tetrazol-5-yl;

R7 = H, COOH, COOA, CONH2, CONHA, CONAA1, NH2, NHA, NAA1, NHCOA, NHCOOA, OH or OA;

R8 = A, 3-7C cycloalkyl, 4-8C alkylenecycloalkyl or 2-8C alkenyl;

R9 = 1-10C alkyl, 3-7C cycloalkyl, 4-8C alkylenecycloalkyl or 2-8C alkenyl (all optionally having 1-3 CH2 replaced by O, S, SO, SO2, NH, NMe, NEt and/or CH=CH; and optionally substituted (os) by 1-7 F and/or Cl and/or by R7);

Y' = 1-10C alkylene or 2-8C alkenylene (both optionally having 1-3 CH2 replaced by O, S, SO, SO2, NH or NR10; and os by 1-7 F and/or Cl);

A, A1 = 1-10C alkyl or 2-8C alkenyl (both optionally having 1-3 CH2 replaced by O, S, SO, SO2, NH or NR10; and os by 1-7 F and/or Cl); or Ar or Het;

A + A1 = 2-7C alkylene (optionally having 1-3 CH2 replaced by O, S, SO, SO2, NH or NR9);

A2, A3 = direct bond; or 1-10C alkylene, 2-8C alkenylene or 3-7C cycloalkylene (all optionally having 1-3 CH2 replaced by O, S, SO, SO2, NH or NR9; and os by 1-7 F and/or Cl);

A2+A3 = 2-7C alkylene (optionally having 1-3 CH2 replaced by O, S, SO, SO2, NH, NR9, NHCOR9 or NHCOOR9);

Ar = phenyl, naphthyl, fluorenyl or biphenylyl (all os by 1-3 of halo, R11, OR10, N(R10)2, NO2, CN, COOR10, CON(R10)2, NR10COR10, NR10CON(R10)2, NR10SO2A, COR10, SO2N(R10)2 or S(O)mR11);

R10 = H or 1-6C alkyl;

R11 = 1-6C alkyl;

Het = mono- or bicyclic, saturated, unsaturated or aromatic heterocycle containing 1 or 2 of N, O and/or S (os by 1 or 2 of =O, halo, R11, OR10, N(R10)2, NO2, CN, COOR10, CON(R10)2, NR10COR10, NR10CON(R10)2, NR10SO2R11, COR10, SO2N(R10)2 or S(O)mR11);

m = 0-2;

n = 0-4.

An INDEPENDENT CLAIM is also included for the preparation of (I).

ACTIVITY - Antiasthmatic; Antiallergic; Antiinflammatory; Dermatological; Antipsoriatic; Immunosuppressive; Antirheumatic; Antiarthritic; Neuroprotective; Antidiabetic; Antiulcer; Osteopathic;

Immunomodulator; Cytostatic; Antibacterial; Nootropic; Antiarteriosclerotic; Anti-HIV; Cardiant; Vasotropic; Antigout; Analgesic; Antipyretic; Ophthalmological; Antianemic; Hepatotropic; Nephrotropic; Hypotensive; Antidepressant; Antiparkinsonian; Antiaddictive; Virucide; Fungicide.

MECHANISM OF ACTION - Phosphodiesterase IV (PDE IV) Inhibitor.

USE - (I) Are PDE IV inhibitors, used for treating diseases involving PDE IV-mediated regulation of the activation and degranulation of eosinophils, specifically asthma, allergy, chronic bronchitis, atopic dermatitis, psoriasis, other skin diseases, inflammatory diseases, autoimmune diseases (e.g. rheumatoid arthritis, multiple sclerosis, Crohn's disease, diabetes or ulcerative colitis), osteoporosis, transplant rejection reactions, cachexia, tumor growth or metastasis, sepsis, memory disorders, atherosclerosis, AIDS, myocardial diseases (specifically of inflammatory and immunological type), coronary heart disease, (ir)reversible myocardial ischemia/reperfusion damage, acute or chronic heart failure or restenosis (including in-stent or stent-in-stent restenosis) (all claimed). Numerous more specific diseases to be treated are specified in the claims, e.g.: several specific types of asthma, bronchitis, bronchiectasis and other obstructive/inflammatory respiratory disorders (e.g. emphysema, dust in the lungs, chronic eosinophilic pneumonia, chronic obstructive pulmonary disease or broncho-pneumonic aspergillosis); allergic rhinitis, sinusitis, allergic dermatitis, allergic or atopic eczema, nettle rash or urticaria; various types of rheumatoid arthritis (e.g. acute gout arthritis, osteoarthritis, psoriatic arthritis or spondylarthritis); gout; pain or fever associated with inflammation; various types of conjunctivitis or uveitis; several types of autoimmune disease (e.g. hemolytic or aplastic anemia, systemic lupus erythematosus, chronic-active hepatitis, myasthenia gravis, alveolitis, primary biliary cirrhosis, type I diabetes mellitus, keratoconjunctivitis sicca, glomerulonephritis, dandruff or pemphigus); irritable bowel disease; liver damage; pulmonary hypertension; CNS disorders (specifically depression, Parkinson's disease, learning or memory deficiency, tardive dyskinesia, drug addiction or various types of dementia); and TNF-alpha-associated viral, yeast or fungal infections (e.g. HIV-1, HIV-2, HIV-3, cytomegalovirus, influenza virus or herpes virus infections); or chronic lymphocytic leukemia.

ADVANTAGE - (I) Are selective and well tolerated PDE IV inhibitors.

MANUAL CODE: CPI: B04-A06; B04-H06B; B04-L05C; B06-A01; B06-D09; B06-D18; B07-A01; B07-B01; B07-D10; B07-F01; B10-D03; B14-A01; B14-A02; B14-A04; B14-C01; B14-C02; B14-C03; B14-C04; B14-C09; B14-D07A; B14-E10C; B14-E11; B14-F01; B14-F03; B14-F05; B14-F07; B14-G01B; B14-G02A; B14-G02C; B14-G02D; B14-H01; B14-J01; B14-J05; B14-K01; B14-M01C; B14-N01; B14-N02; B14-N03; B14-N04; B14-N10; B14-N12; B14-N16; B14-N17; B14-R02; B14-S01; B14-S04; C04-A06; C04-H06B; C04-L05C; C06-A01; C06-D09; C06-D18; C07-A01; C07-B01; C07-D10; C07-F01; C10-D03; C14-A01; C14-A02; C14-A04; C14-C01; C14-C02; C14-C03; C14-C04; C14-C09; C14-D07A; C14-E10C; C14-E11; C14-F01; C14-F03; C14-F05; C14-F07; C14-G01B; C14-G02A; C14-G02C; C14-G02D; C14-H01; C14-J01; C14-J05; C14-K01; C14-M01C; C14-N01; C14-N02; C14-N03; C14-N04; C14-N10; C14-N12; C14-N16; C14-N17; C14-R02; C14-S01; C14-S04; D08-B03

AN 2004-099097 [10] WPIX

DC B02; B03; B05; C02; C03; D21

IC ICM C07D; C07D417-06; C07D417-14

ICS A61K; A61P; A61K031-501; A61P001-00; A61P001-04; A61P001-16; A61P011-00; A61P011-02; A61P011-06; A61P011-08; A61P013-08; A61P013-12; A61P017-00; A61P017-02; A61P017-04; A61P017-06; A61P019-02; A61P019-06; A61P019-10; A61P021-04; A61P025-00; A61P025-14; A61P025-16; A61P025-24; A61P025-28; A61P027-02; A61P027-14; A61P029-00; A61P003-10; A61P031-04; A61P031-10;

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IPCI A61K0031-50 [I,A]; A61K0031-50 [I,A]; A61K0031-50 [I,C]; A61P0011-00 [I,C]; A61P0011-00 [I,C]; A61P0011-06 [I,A]; A61P0011-06 [I,A]; A61P0019-00 [I,C]; A61P0019-00 [I,C]; A61P0019-02 [I,A]; A61P0019-02 [I,A]; A61P0019-10 [I,A]; A61P0019-10 [I,A]; A61P0029-00 [I,A]; A61P0029-00 [I,A]; A61P0029-00 [I,C]; A61P0035-00 [I,A]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; C07D0417-00 [I,C]; C07D0417-00 [I,C]; C07D0417-00 [I,C]; C07D0417-06 [I,A]; C07D0417-06 [I,A]; C07D0417-14 [I,A]; C07D0417-14 [I,A]

IPCR A61K0031-501 [I,A]; A61K0031-501 [I,C]; A61P0001-00 [I,A]; A61P0001-00 [I,C]; A61P0001-04 [I,A]; A61P0001-16 [I,A]; A61P0011-00 [I,A]; A61P0011-00 [I,C]; A61P0011-02 [I,A]; A61P0011-06 [I,A]; A61P0011-08 [I,A]; A61P0013-00 [I,C]; A61P0013-08 [I,A]; A61P0013-12 [I,A]; A61P0017-00 [I,A]; A61P0017-00 [I,C]; A61P0017-02 [I,A]; A61P0017-04 [I,A]; A61P0017-06 [I,A]; A61P0019-00 [I,C]; A61P0019-02 [I,A]; A61P0019-06 [I,A]; A61P0019-10 [I,A]; A61P0021-00 [I,C]; A61P0021-04 [I,A]; A61P0025-00 [I,A]; A61P0025-00 [I,C]; A61P0025-14 [I,A]; A61P0025-16 [I,A]; A61P0025-24 [I,A]; A61P0025-28 [I,A]; A61P0027-00 [I,C]; A61P0027-02 [I,A]; A61P0027-14 [I,A]; A61P0029-00 [I,A]; A61P0029-00 [I,C]; A61P0003-00 [I,C]; A61P0003-10 [I,A]; A61P0031-00 [I,C]; A61P0031-04 [I,A]; A61P0031-10 [I,A]; A61P0031-16 [I,A]; A61P0031-18 [I,A]; A61P0031-20 [I,A]; A61P0031-22 [I,A]; A61P0033-00 [I,C]; A61P0033-02 [I,A]; A61P0033-06 [I,A]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; A61P0037-00 [I,C]; A61P0037-02 [I,A]; A61P0037-06 [I,A]; A61P0037-08 [I,A]; A61P0043-00 [I,A]; A61P0043-00 [I,C]; A61P0005-00 [I,C]; A61P0005-14 [I,A]; A61P0007-00 [I,A]; A61P0007-00 [I,C]; A61P0007-04 [I,A]; A61P0007-06 [I,A]; A61P0009-00 [I,A]; A61P0009-00 [I,C]; A61P0009-10 [I,A]; C07D0417-00 [I,C]; C07D0417-06 [I,A]; C07D0417-14 [I,A]; A61K0031-50 [I,A]; A61K0031-50 [I,C]

MC CPI: B04-A06; B04-H06B; B04-L05C; B06-A01; B06-D09; B06-D18; B07-A01; B07-B01; B07-D10; B07-F01; B10-D03; B14-A01; B14-A02; B14-A04; B14-C01; B14-C02; B14-C03; B14-C04; B14-C09; B14-D07A; B14-E10C; B14-E11; B14-F01; B14-F03; B14-F05; B14-F07; B14-G01B; B14-G02A; B14-G02C; B14-G02D; B14-H01; B14-J01; B14-J05; B14-K01; B14-M01C; B14-N01; B14-N02; B14-N03; B14-N04; B14-N10; B14-N12; B14-N16; B14-N17; B14-R02; B14-S01; B14-S04; C04-A06; C04-H06B; C04-L05C; C06-A01; C06-D09; C06-D18; C07-A01; C07-B01; C07-D10; C07-F01; C10-D03; C14-A01; C14-A02; C14-A04; C14-C01; C14-C02; C14-C03; C14-C04; C14-C09; C14-D07A; C14-E10C; C14-E11; C14-F01; C14-F03; C14-F05; C14-F07; C14-G01B; C14-G02A; C14-G02C; C14-G02D; C14-H01; C14-J01; C14-J05; C14-K01; C14-M01C; C14-N01; C14-N02; C14-N03; C14-N04; C14-N10; C14-N12; C14-N16; C14-N17; C14-R02; C14-S01; C14-S04; D08-B03

CMC UPB 20060121

DRN: 0163-U 0180-U 1218-U

DCR: 60080-U 6284-U 86977-U

M1 *23* M423 M431 M782 Q233 M905

DCN: RA063L-K RA063L-M

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DCR: 122552-K 122552-M

M2 *01* F011 F012 F013 F014 F015 F019 F530 F570 F710 G013 G015 G100 H2 H211 H5 H542 H8 J0 J011 J3 J311 K0 K6 K630 L1 L141 M1 M113 M119 M210 M211 M212 M240 M272 M281 M282 M320 M413 M431 M510 M523 M532 M540 M710 M720 M782 N225 N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422 P423 P431 P433 P434 P446 P451 P510 P517 P520 P522

P526 P616 P625 P631 P632 P633 P646 P714 P721 P722 P723 P738 P811
P812 P814 P816 P820 P822 P921 P922 P924 P943 Q233 M905 M904
RIN: 00061
DCN: RACVZP-M RACVZP-N RACVZP-P RACVZP-T
DCR: 835721-M 835721-N 835721-P 835721-T

M2 *02* F011 F012 F013 F014 F015 F530 F710 G013 G015 G100 H2 H211 H5
H542 H8 J0 J011 J3 J311 K0 K6 K630 L1 L141 L199 M1 M113 M119
M210 M211 M212 M240 M272 M281 M282 M320 M413 M431 M510 M522 M532
M540 M710 M720 M782 N225 N241 N261 N331 N512 P210 P220 P241 P411
P420 P421 P422 P423 P431 P433 P434 P446 P451 P510 P517 P520 P522
P526 P616 P625 P631 P632 P633 P646 P714 P721 P722 P723 P738 P811
P812 P814 P816 P820 P822 P921 P922 P924 P943 Q233 M905 M904
DCN: RACVZO-M RACVZO-N RACVZO-P RACVZO-T
DCR: 835720-M 835720-N 835720-P 835720-T

M2 *03* F011 F012 F013 F014 F015 F530 F710 G013 G015 G100 H1 H100 H141
H2 H211 H5 H542 H8 J0 J011 J3 J311 M1 M113 M119 M210 M211 M212
M240 M272 M281 M282 M320 M413 M431 M510 M522 M532 M540 M710 M720
M782 N225 N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422
P423 P431 P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625
P631 P632 P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816
P820 P822 P921 P922 P924 P943 Q233 M905 M904
DCN: RACVZN-M RACVZN-N RACVZN-P RACVZN-T
DCR: 835719-M 835719-N 835719-P 835719-T

M2 *04* F011 F012 F013 F014 F015 F530 F710 G013 G015 G100 H2 H211 H5
H543 H8 J0 J011 J3 J311 M1 M113 M119 M210 M211 M212 M240 M272
M281 M283 M320 M413 M431 M510 M522 M532 M540 M710 M720 M782 N225
N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422 P423 P431
P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625 P631 P632
P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816 P820 P822
P921 P922 P924 P943 Q233 M905 M904
DCN: RACVZM-M RACVZM-N RACVZM-P RACVZM-T
DCR: 835718-M 835718-N 835718-P 835718-T

M2 *05* F011 F012 F013 F014 F015 F530 F710 G010 G015 G100 H2 H211 H5
H542 H8 J0 J011 J3 J311 M1 M113 M119 M210 M211 M212 M240 M272
M281 M282 M320 M413 M431 M510 M522 M532 M540 M710 M720 M782 N225
N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422 P423 P431
P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625 P631 P632
P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816 P820 P822
P921 P922 P924 P943 Q233 M905 M904
DCN: RACVZI-M RACVZI-N RACVZI-P RACVZI-T
DCR: 835714-M 835714-N 835714-P 835714-T

M2 *06* F011 F012 F013 F014 F015 F019 F211 F530 F710 G015 G030 G111 G553
H2 H211 H5 H542 H8 J0 J011 J3 J311 M1 M113 M116 M123 M141 M210
M211 M240 M272 M281 M320 M413 M431 M510 M523 M531 M541 M710 M720
M782 N225 N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422
P423 P431 P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625
P631 P632 P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816
P820 P822 P921 P922 P924 P943 Q233 M905 M904
DCN: RACVZH-M RACVZH-N RACVZH-P RACVZH-T
DCR: 835713-M 835713-N 835713-P 835713-T

M2 *07* F011 F012 F013 F014 F015 F019 F211 F530 F710 G015 G100 H2 H211
H5 H542 H8 J0 J011 J3 J311 M1 M113 M116 M210 M211 M213 M232 M240
M272 M281 M282 M320 M413 M431 M510 M523 M531 M540 M710 M720 M782
N225 N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422 P423
P431 P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625 P631
P632 P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816 P820
P822 P921 P922 P924 P943 Q233 M905 M904
DCN: RACVZG-M RACVZG-N RACVZG-P RACVZG-T
DCR: 835712-M 835712-N 835712-P 835712-T

M2 *08* F011 F012 F013 F014 F015 F019 F211 F530 F710 G015 G100 H2 H211

H5 H542 H8 J0 J011 J3 J311 M1 M113 M116 M210 M211 M212 M240 M272
M281 M282 M320 M413 M431 M510 M523 M531 M540 M710 M720 M782 N225
N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422 P423 P431
P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625 P631 P632
P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816 P820 P822
P921 P922 P924 P943 Q233 M905 M904
DCN: RACVZF-M RACVZF-N RACVZF-P RACVZF-T
DCR: 835711-M 835711-N 835711-P 835711-T

M2 *09* F011 F012 F013 F014 F015 F019 F530 F551 F710 G015 G030 G111 G553
H2 H211 H5 H542 H8 J0 J011 J3 J311 M1 M113 M116 M123 M141 M210
M211 M240 M272 M281 M320 M413 M431 M510 M523 M531 M541 M710 M720
M782 N225 N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422
P423 P431 P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625
P631 P632 P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816
P820 P822 P921 P922 P924 P943 Q233 M905 M904
DCN: RACVZE-M RACVZE-N RACVZE-P RACVZE-T
DCR: 835710-M 835710-N 835710-P 835710-T

M2 *10* F011 F012 F013 F014 F015 F019 F530 F551 F710 G015 G100 H2 H211
H5 H542 H8 J0 J011 J3 J311 M1 M113 M116 M210 M211 M213 M232 M240
M272 M281 M282 M320 M413 M431 M510 M523 M531 M540 M710 M720 M782
N225 N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422 P423
P431 P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625 P631
P632 P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816 P820
P822 P921 P922 P924 P943 Q233 M905 M904
DCN: RACVZD-M RACVZD-N RACVZD-P RACVZD-T
DCR: 835709-M 835709-N 835709-P 835709-T

M2 *11* F011 F012 F013 F014 F015 F019 F530 F551 F710 G015 G100 H2 H211
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M281 M282 M320 M413 M431 M510 M523 M531 M540 M710 M720 M782 N225
N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422 P423 P431
P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625 P631 P632
P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816 P820 P822
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DCN: RACVZC-M RACVZC-N RACVZC-P RACVZC-T
DCR: 835708-M 835708-N 835708-P 835708-T

M2 *12* F011 F012 F013 F014 F015 F019 F431 F530 F710 G015 G030 G111 G553
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M211 M240 M272 M281 M320 M413 M431 M510 M523 M531 M541 M710 M720
M782 N225 N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422
P423 P431 P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625
P631 P632 P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816
P820 P822 P921 P922 P924 P943 Q233 M905 M904
DCN: RACVZB-M RACVZB-N RACVZB-P RACVZB-T
DCR: 835707-M 835707-N 835707-P 835707-T

M2 *13* F011 F012 F013 F014 F015 F019 F431 F530 F710 G015 G100 H2 H211
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M272 M281 M282 M320 M413 M431 M510 M523 M531 M540 M710 M720 M782
N225 N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422 P423
P431 P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625 P631
P632 P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816 P820
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DCN: RACVZA-M RACVZA-N RACVZA-P RACVZA-T
DCR: 835706-M 835706-N 835706-P 835706-T

M2 *14* F011 F012 F013 F014 F015 F019 F431 F530 F710 G015 G100 H2 H211
H5 H542 H8 J0 J011 J3 J311 M1 M113 M116 M210 M211 M212 M240 M272
M281 M282 M320 M413 M431 M510 M523 M531 M540 M710 M720 M782 N225
N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422 P423 P431
P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625 P631 P632
P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816 P820 P822
P921 P922 P924 P943 Q233 M905 M904

DCN: RACVZ9-M RACVZ9-N RACVZ9-P RACVZ9-T
DCR: 835705-M 835705-N 835705-P 835705-T
M2 *15* F011 F012 F013 F014 F015 F019 F431 F530 F710 G015 G030 G111 G553 H2 H211 H5 H542 H8 J0 J011 J3 J311 M1 M113 M116 M123 M141 M210 M211 M240 M272 M281 M320 M413 M431 M510 M523 M531 M541 M710 M720 M782 N225 N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422 P423 P431 P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625 P631 P632 P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816 P820 P822 P921 P922 P924 P943 Q233 M905 M904
DCN: RACVZ8-M RACVZ8-N RACVZ8-P RACVZ8-T
DCR: 835704-M 835704-N 835704-P 835704-T
M2 *16* F011 F012 F013 F014 F015 F019 F431 F530 F710 G015 G100 H2 H211 H5 H542 H8 J0 J011 J3 J311 M1 M113 M116 M210 M211 M213 M232 M240 M272 M281 M282 M320 M413 M431 M510 M523 M531 M540 M710 M720 M782 N225 N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422 P423 P431 P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625 P631 P632 P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816 P820 P822 P921 P922 P924 P943 Q233 M905 M904
DCN: RACVZ7-M RACVZ7-N RACVZ7-P RACVZ7-T
DCR: 835703-M 835703-N 835703-P 835703-T
M2 *17* F011 F012 F013 F014 F015 F019 F431 F530 F710 G015 G100 H2 H211 H5 H542 H8 J0 J011 J3 J311 M1 M113 M116 M210 M211 M212 M240 M272 M281 M282 M320 M413 M431 M510 M523 M531 M540 M710 M720 M782 N225 N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422 P423 P431 P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625 P631 P632 P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816 P820 P822 P921 P922 P924 P943 Q233 M905 M904
DCN: RACVZ6-M RACVZ6-N RACVZ6-P RACVZ6-T
DCR: 835702-M 835702-N 835702-P 835702-T
M2 *18* F011 F012 F013 F014 F015 F019 F431 F530 F710 G015 G100 H2 H211 H5 H542 H8 J0 J011 J3 J311 K0 K7 K742 M1 M113 M116 M210 M211 M212 M240 M272 M281 M282 M320 M413 M431 M510 M523 M531 M540 M710 M720 M782 N225 N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422 P423 P431 P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625 P631 P632 P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816 P820 P822 P921 P922 P924 P943 Q233 M905 M904
DCN: RACVZ5-M RACVZ5-N RACVZ5-P RACVZ5-T
DCR: 835701-M 835701-N 835701-P 835701-T
M2 *19* F011 F012 F013 F014 F015 F019 F431 F530 F710 G015 G100 H2 H211 H5 H542 H8 J0 J011 J3 J311 K0 K7 K742 M1 M113 M116 M210 M211 M213 M232 M240 M272 M281 M282 M320 M413 M431 M510 M523 M531 M540 M710 M720 M782 N225 N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422 P423 P431 P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625 P631 P632 P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816 P820 P822 P921 P922 P924 P943 Q233 M905 M904
DCN: RACVZ4-M RACVZ4-N RACVZ4-P RACVZ4-T
DCR: 835700-M 835700-N 835700-P 835700-T
M2 *20* F011 F012 F013 F014 F015 F019 F431 F530 F710 G015 G030 G111 G553 H2 H211 H5 H542 H8 J0 J011 J3 J311 K0 K7 K742 M1 M113 M116 M123 M141 M210 M211 M240 M272 M281 M320 M413 M431 M510 M523 M531 M541 M710 M720 M782 N225 N241 N261 N331 N512 P210 P220 P241 P411 P420 P421 P422 P423 P431 P433 P434 P446 P451 P510 P517 P520 P522 P526 P616 P625 P631 P632 P633 P646 P714 P721 P722 P723 P738 P811 P812 P814 P816 P820 P822 P921 P922 P924 P943 Q233 M905 M904
DCN: RACVZ3-M RACVZ3-N RACVZ3-P RACVZ3-T
DCR: 835699-M 835699-N 835699-P 835699-T
M2 *21* C216 C316 D010 D019 D020 D021 D022 D029 D040 D049 D140 D150 F010 F011 F012 F013 F015 F016 F019 F020 F021 F029 F211 F212 F410 F499 F530 F570 F599 F710 G001 G002 G003 G010 G011 G012 G013 G014 G015 G016 G019 G020 G021 G022 G029 G030 G031 G039 G040 G050 G100 G111

G112 G113 G221 G299 G310 G399 G553 G563 H100 H101 H102 H103 H121
H122 H123 H141 H142 H143 H161 H162 H163 H181 H182 H183 H2 H211
H212 H213 H321 H322 H323 H341 H342 H343 H361 H362 H363 H401 H402
H403 H404 H405 H421 H422 H423 H424 H441 H442 H443 H444 H461 H462
H463 H464 H481 H482 H483 H484 H521 H522 H523 H541 H542 H543 H561
H562 H563 H581 H582 H583 H594 H599 H600 H608 H609 H621 H622 H623
H641 H642 H643 H661 H662 H663 H713 H715 H716 H721 H722 H723 J011
J012 J013 J014 J111 J112 J113 J131 J132 J133 J151 J152 J153 J171
J172 J173 J211 J212 J221 J222 J231 J232 J241 J242 J251 J252 J261
J262 J271 J272 J273 J311 J312 J321 J322 J331 J332 J341 J342 J351
J352 J361 J362 J371 J372 J373 J411 J5 J521 J522 J523 J581 K442
K499 K620 K630 K640 K699 K810 K820 K830 K850 K899 K910 K920 K999
L141 L199 L410 L431 L432 L462 L463 L472 L499 L532 L541 L560 L599
L640 L660 L699 L9 L941 L999 M1 M111 M113 M115 M116 M119 M123
M125 M126 M129 M131 M135 M136 M137 M139 M141 M142 M143 M146 M147
M149 M210 M211 M212 M213 M214 M215 M216 M220 M221 M222 M223 M224
M225 M226 M231 M232 M233 M240 M262 M271 M272 M273 M280 M281 M282
M283 M311 M312 M313 M314 M315 M316 M321 M322 M323 M331 M332 M333
M340 M342 M349 M372 M373 M381 M382 M383 M391 M392 M393 M412 M413
M431 M510 M511 M512 M513 M522 M523 M530 M531 M532 M533 M540 M541
M542 M543 M710 M720 M782 N225 N241 N261 N331 N512 P210 P220 P241
P411 P420 P421 P422 P423 P431 P433 P434 P446 P451 P510 P517 P520
P522 P526 P616 P625 P631 P632 P633 P646 P714 P721 P722 P723 P738
P811 P812 P814 P816 P820 P822 P921 P922 P924 P943 Q233 M905
M904
RIN: 00061 01662
MCN: 0119-00002-M 0119-00002-N 0119-00002-P 0119-00002-T

M2 *22* C216 C316 D010 D019 D020 D021 D022 D029 D040 D049 D140 D150 F010
F011 F012 F013 F015 F019 F020 F021 F029 F211 F212 F410 F499 F530
F570 F599 F710 G001 G002 G003 G010 G011 G012 G013 G014 G015 G016
G019 G020 G021 G022 G029 G030 G031 G039 G040 G050 G100 G111 G112
G113 G221 G299 G310 G399 G553 G563 H100 H101 H102 H103 H121 H122
H123 H141 H142 H143 H161 H162 H163 H181 H182 H183 H2 H211 H212
H213 H321 H322 H323 H341 H342 H343 H361 H362 H363 H401 H402 H403
H404 H405 H421 H422 H423 H424 H441 H442 H443 H444 H461 H462 H463
H464 H481 H482 H483 H484 H521 H522 H523 H541 H542 H543 H561 H562
H563 H581 H582 H583 H594 H599 H600 H608 H609 H621 H622 H623 H641
H642 H643 H661 H662 H663 H713 H715 H716 H721 H722 H723 J0 J011
J012 J013 J014 J111 J112 J113 J131 J132 J133 J151 J152 J153 J171
J172 J173 J211 J212 J221 J222 J231 J232 J241 J242 J251 J252 J261
J262 J271 J272 J273 J3 J311 J312 J321 J322 J331 J332 J341 J342
J351 J352 J361 J362 J371 J372 J373 J411 J521 J522 J523 J581 K442
K499 K620 K630 K640 K699 K810 K820 K830 K850 K899 K910 K920 K999
L141 L199 L410 L431 L432 L462 L463 L472 L499 L532 L541 L560 L599
L640 L660 L699 L941 L999 M1 M111 M113 M115 M116 M119 M123 M125
M126 M129 M131 M135 M136 M137 M139 M141 M142 M143 M146 M147 M149
M210 M211 M212 M213 M214 M215 M216 M220 M221 M222 M223 M224 M225
M226 M231 M232 M233 M240 M262 M271 M272 M273 M280 M281 M282 M283
M311 M312 M313 M314 M315 M316 M320 M321 M322 M323 M331 M332 M333
M340 M342 M349 M372 M373 M381 M382 M383 M391 M392 M393 M412 M413
M431 M510 M511 M512 M513 M522 M523 M530 M531 M532 M533 M540 M541
M542 M543 M710 M720 M782 N225 N241 N261 N331 N512 P210 P220 P241
P411 P420 P421 P422 P423 P431 P433 P434 P446 P451 P510 P517 P520
P522 P526 P616 P625 P631 P632 P633 P646 P714 P721 P722 P723 P738
P811 P812 P814 P816 P820 P822 P921 P922 P924 P943 Q233 M905
M904
RIN: 00061 01662
MCN: 0119-00001-M 0119-00001-N 0119-00001-P 0119-00001-T

M2 *25* G015 G100 H4 H401 H441 H5 H541 H7 H721 H8 J0 J011 J3 J371 M210
M211 M220 M223 M232 M262 M272 M281 M311 M321 M342 M373 M391 M414

M431 M510 M520 M531 M540 M782 Q233 M905 M904
DCN: R03442-K R03442-M
DCR: 89965-K 89965-M

M2 *26* D011 D016 D023 D024 D026 D030 E330 E350 H1 H181 H2 H201 H4 H402 H421 H461 H5 H541 H8 J0 J013 J2 J211 J251 J261 M1 M116 M210 M211 M212 M240 M262 M272 M273 M281 M282 M283 M320 M412 M431 M512 M520 M530 M540 M782 M800 Q233 M905 M904
RIN: 11065 13275
DCN: R04079-K R04079-M R17068-K R17068-M
DCR: 110145-K 110145-M

M2 *27* D011 D920 J5 J521 L9 L941 M280 M320 M412 M431 M511 M520 M530 M540 M782 Q233 M905 M904 M910
RIN: 01174
DCN: R01218-K R01218-M R04867-K R04867-M RA3MZJ-K RA3MZJ-M
DCR: 375800-K 375800-M 86977-K 86977-M 86977-U

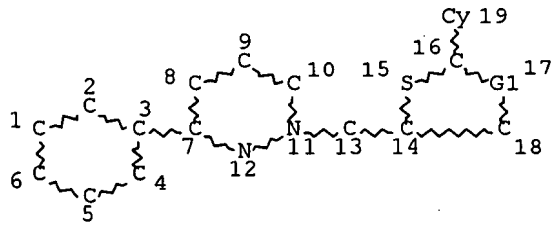
M2 *28* D012 D013 D940 G013 G100 H1 H101 H103 H122 H141 J0 J013 J1 J172 J3 J331 L9 L910 M210 M211 M273 M281 M311 M313 M321 M332 M342 M343 M349 M373 M381 M391 M412 M431 M511 M520 M531 M540 M782 Q233 M905 M904 M910
DCN: R00180-K R00180-M
DCR: 60080-K 60080-M 60080-U

M2 *29* C316 F012 F013 F014 F112 G010 G013 G100 J5 J521 K0 K4 K442 L9 L942 M1 M113 M119 M210 M211 M271 M281 M320 M413 M431 M510 M521 M532 M540 M782 Q233 M905 M904
DCN: RA027J-K RA027J-M RA06CV-K RA06CV-M
DCR: 129270-K 129270-M 208737-K 208737-M

M2 *30* A111 A960 C710 D013 D019 D021 D029 D120 D199 H4 H401 H481 H5 H542 H8 J0 J012 J1 J112 J5 J522 M280 M313 M321 M332 M343 M383 M391 M411 M431 M512 M520 M530 M540 M630 M782 Q233 M905 M904
DCN: R04193-K R04193-M
DCR: 91814-K 91814-M

M2 *31* D015 D932 H2 H212 J5 J522 L9 L910 M210 M211 M273 M282 M320 M412 M431 M511 M520 M530 M540 M782 Q233 M905 M904 M910
DCN: R00163-K R00163-M R12974-K R12974-M
DCR: 6284-K 6284-M 6284-U

```
=> => d que stat l7
L5              STR
```



```
VAR G1=C/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  19

STEREO ATTRIBUTES: NONE
L7            21 SEA FILE=REGISTRY SSS FUL L5

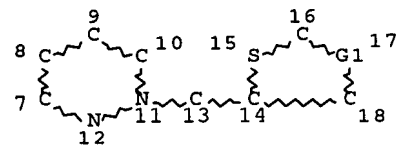
100.0% PROCESSED    3813 ITERATIONS                          21 ANSWERS
SEARCH TIME: 00.00.01


=> d que nos l8
L5              STR
L7            21 SEA FILE=REGISTRY SSS FUL L5
L8              ANALYZE  PLU=ON  L7 1- LC :       4 TERMS


=> d l8 1-
L8          ANALYZE L7 1- LC :       4 TERMS

TERM #   # OCC  # DOC  % DOC LC
------ ------- ------ ------ ---------------
     1      21     21 100.00 CA
     2      21     21 100.00 CAPLUS
     3      21     21 100.00 TOXCENTER
     4      21     21 100.00 USPATFULL
*********  END OF L8 ***


=> d que stat l15
L13             STR
```



```
VAR G1=C/N
NODE ATTRIBUTES:
NSPEC   IS RC     AT  13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  12

STEREO ATTRIBUTES: NONE
L15          85 SEA FILE=REGISTRY SSS FUL L13

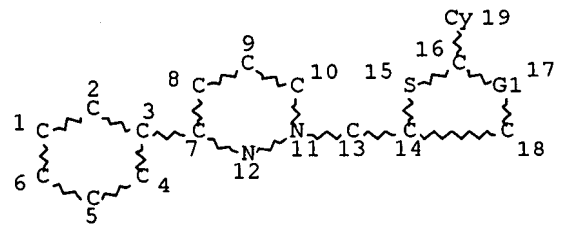
100.0% PROCESSED     661 ITERATIONS                              85 ANSWERS
SEARCH TIME: 00.00.01


=> d que nos l16
L13             STR
L15          85 SEA FILE=REGISTRY SSS FUL L13
L16             ANALYZE  PLU=ON  L15 1- LC :       7 TERMS


=> d l16 1-
L16         ANALYZE L15 1- LC :       7 TERMS

TERM #   # OCC  # DOC  % DOC LC
------ ------- ------ ------ ---------------
     1      85     85 100.00 CA
     2      85     85 100.00 CAPLUS
     3      65     65  76.47 USPATFULL
     4      26     26  30.59 TOXCENTER
     5      12     12  14.12 BEILSTEIN
     6       7      7   8.24 USPAT2
     7       3      3   3.53 CASREACT
*********  END OF L16***


=> d que l35
L5              STR
```

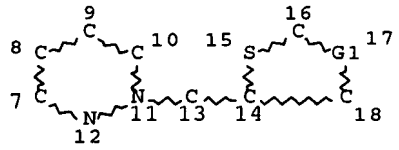



```
VAR G1=C/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
```

```
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  19

STEREO ATTRIBUTES: NONE
L7            21 SEA FILE=REGISTRY SSS FUL L5
L13              STR
```



```
VAR G1=C/N
NODE ATTRIBUTES:
NSPEC    IS RC     AT  13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  12

STEREO ATTRIBUTES: NONE
L15           85 SEA FILE=REGISTRY SSS FUL L13
L21              QUE  ABB=ON  PLU=ON  AY<2004 OR PY<2004 OR PRY<2004 OR MY
                 <2004 OR REVIEW/DT
L24              QUE  ABB=ON  PLU=ON  ?PHOSPHODIESTERAS? OR (?PHOSPHO(W)DI
                 ESTERAS?) OR (?PHOSPHODI(W)ESTERAS?)
L27              QUE  ABB=ON  PLU=ON  ?PYRIDAZIN?
L28              QUE  ABB=ON  PLU=ON  ?THIAZOL? OR ?THIOPHEN?
L29            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7
L30           32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15
L31           32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L29 OR L30)
L32           31 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L31 AND (L24 OR L27 OR L28)
L33           32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L31 OR L32
L34           31 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L33 AND L21
L35           32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L33 OR L34)


=> d his l43

     (FILE 'USPATFULL, USPAT2' ENTERED AT 11:51:32 ON 20 DEC 2006)
L43            2 S L37 OR L40 OR L42

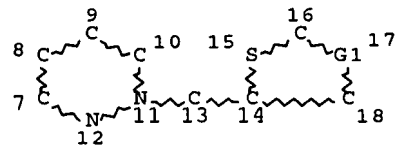
=> d que nos l43
L5               STR
L7            21 SEA FILE=REGISTRY SSS FUL L5
L13              STR
L15           85 SEA FILE=REGISTRY SSS FUL L13
L24              QUE  ABB=ON  PLU=ON  ?PHOSPHODIESTERAS? OR (?PHOSPHO(W)DI
                 ESTERAS?) OR (?PHOSPHODI(W)ESTERAS?)
L37            1 SEA L7
L38           42 SEA L15
L39           42 SEA (L37 OR L38)
```

```
L40             1 SEA L39 AND L24/TI,IT,CC,CT,ST,STP,BI,AB
L41            36 SEA L39 AND A61?/IPC
L42             1 SEA L41 AND A61P?/IPC
L43             2 SEA L37 OR L40 OR L42


=> d que nos l46
L5                STR
L7             21 SEA FILE=REGISTRY SSS FUL L5
L13               STR
L15            85 SEA FILE=REGISTRY SSS FUL L13
L44             1 SEA FILE=TOXCENTER ABB=ON  PLU=ON  L7
L45             6 SEA FILE=TOXCENTER ABB=ON  PLU=ON  L15
L46             6 SEA FILE=TOXCENTER ABB=ON  PLU=ON  (L44 OR L45)


=> d que nos l48
L13               STR
L15            85 SEA FILE=REGISTRY SSS FUL L13
L23             3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L15 AND CASREACT/LC
L48             3 SEA FILE=CASREACT ABB=ON  PLU=ON  L23


=> d que stat l49
L13               STR
```




```
VAR G1=C/N
NODE ATTRIBUTES:
NSPEC   IS RC     AT  13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  12

STEREO ATTRIBUTES: NONE
L49            17 SEA FILE=BEILSTEIN SSS FUL L13

100.0% PROCESSED      31 ITERATIONS                                 17 ANSWERS
SEARCH TIME: 00.00.05


=> d his 149-151

     (FILE 'CASREACT' ENTERED AT 11:55:28 ON 20 DEC 2006)
               SAVE TEMP L48 JAI503CRXB/A

     FILE 'STNGUIDE' ENTERED AT 11:56:11 ON 20 DEC 2006

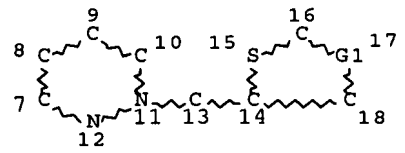
     FILE 'BEILSTEIN' ENTERED AT 11:56:55 ON 20 DEC 2006
```

```
L49          17 S L13 FUL
                SAVE TEMP L49 JAI503BEIP/A
L50           1 S L49 NOT BABSAN/FA
                SELECT L49 1- BABSAN

     FILE 'BABS' ENTERED AT 11:58:18 ON 20 DEC 2006
L51           6 S E13-E18/AN

=> d que l51
L51           6 SEA FILE=BABS ABB=ON  PLU=ON  (5596494/AN OR 6388164/AN OR
                5856247/AN OR 6347066/AN OR 6428743/AN OR 6531693/AN)


=> d que stat l53
L13               STR
```



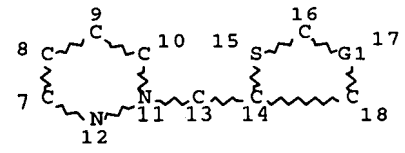
```
VAR G1=C/N
NODE ATTRIBUTES:
NSPEC   IS RC     AT  13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  12

STEREO ATTRIBUTES: NONE
L53           2 SEA FILE=CHEMINFORMRX SSS FUL L13 (     6 REACTIONS)

100.0% DONE      25 VERIFIED       6 HIT RXNS                    2 DOCS
SEARCH TIME: 00.00.04


=> d que stat l55
L13               STR
```



```
VAR G1=C/N
NODE ATTRIBUTES:
NSPEC   IS RC     AT  13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
```

```
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  12

STEREO ATTRIBUTES: NONE
L55          35 SEA FILE=WPIX SSS FUL L13

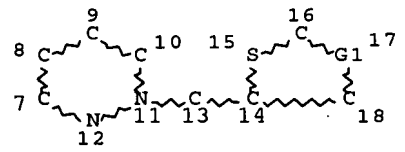
100.0% PROCESSED      40 ITERATIONS                              35 ANSWERS
SEARCH TIME: 00.00.01


=> d his l55-l58

     (FILE 'WPIX' ENTERED AT 12:00:45 ON 20 DEC 2006)
L55          35 S L13 FUL
                SAVE TEMP L55 JAI503WPIS/A
                SELECT L55 1- SDCN
L56          11 S E19-E53/DCN
L57          11 S L55/DCR
L58          11 S L56-L57

=> d que nos l58
L13             STR
L55          35 SEA FILE=WPIX SSS FUL L13
L56          11 SEA FILE=WPIX ABB=ON  PLU=ON  (RACQNP/DCN OR RACVZA/DCN OR
                RACVZB/DCN OR RACVZC/DCN OR RACVZD/DCN OR RACVZE/DCN OR
                RACVZF/DCN OR RACVZG/DCN OR RACVZH/DCN OR RACVZI/DCN OR
                RACVZM/DCN OR RACVZN/DCN OR RACVZO/DCN OR RACVZP/DCN OR
                RACVZ3/DCN OR RACVZ4/DCN OR RACVZ5/DCN OR RACVZ6/DCN OR
                RACVZ7/DCN OR RACVZ8/DCN OR RACVZ9/DCN OR RANV5C/DCN OR
                RANV5G/DCN OR RANV5P/DCN OR RANV5Q/DCN OR RANV6F/DCN OR
                RANV66/DCN OR RA1KDF/DCN OR RA1RZ6/DCN OR RA4W3Q/DCN OR
                RA4XH0/DCN OR RA4X3I/DCN OR RA4X4A/DCN OR RA4X4D/DCN OR
                RA6SZ8/DCN)
L57          11 SEA FILE=WPIX ABB=ON  PLU=ON  L55/DCR
L58          11 SEA FILE=WPIX ABB=ON  PLU=ON  (L56 OR L57)


=> d que stat l95
L13             STR
```



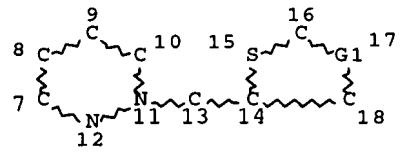

```
VAR G1=C/N
NODE ATTRIBUTES:
NSPEC   IS RC     AT  13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  12
```

STEREO ATTRIBUTES: NONE
L95 57 SEA FILE=MARPAT SSS FUL L13

100.0% PROCESSED 6125 ITERATIONS 57 ANSWERS
SEARCH TIME: 00.00.03

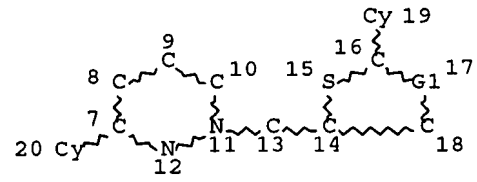
=> d que stat l98
L13 STR



VAR G1=C/N
NODE ATTRIBUTES:
NSPEC IS RC AT 13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE
L95 57 SEA FILE=MARPAT SSS FUL L13
L96 STR



VAR G1=C/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
MLEVEL IS ANY AT 19 20
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L98 2 SEA FILE=MARPAT SUB=L95 SSS FUL L96

100.0% PROCESSED 54 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

```
=> d que l71
L24             QUE  ABB=ON  PLU=ON  ?PHOSPHODIESTERAS? OR (?PHOSPHO(W)DI
                ESTERAS?) OR (?PHOSPHODI(W)ESTERAS?)
L28             QUE  ABB=ON  PLU=ON  ?THIAZOL? OR ?THIOPHEN?
L65             QUE  ABB=ON  PLU=ON  PYRIDAZINES+PFT,OLD,NEW,NT/CT
L66             QUE  ABB=ON  PLU=ON  THIOPHENES+PFT,OLD,NEW,NT/CT
L67             QUE  ABB=ON  PLU=ON  THIAZOLES+PFT,OLD,NEW,NT/CT
L68         257 SEA FILE=MEDLINE ABB=ON  PLU=ON  L65 AND (L66 OR L67 OR L28)
L69             QUE  ABB=ON  PLU=ON  "PHOSPHODIESTERASE INHIBITORS"+PFT,O
                LD,NEW,NT/CT
L70             QUE  ABB=ON  PLU=ON  "PHOSPHODIESTERASES/ANTAGONISTS & IN
                HIBITORS"+PFT,OLD,NEW,NT/CT
L71          11 SEA FILE=MEDLINE ABB=ON  PLU=ON  L68 AND (L24 OR (L69 OR L70))


=> d que l87
L24             QUE  ABB=ON  PLU=ON  ?PHOSPHODIESTERAS? OR (?PHOSPHO(W)DI
                ESTERAS?) OR (?PHOSPHODI(W)ESTERAS?)
L27             QUE  ABB=ON  PLU=ON  ?PYRIDAZIN?
L28             QUE  ABB=ON  PLU=ON  ?THIAZOL? OR ?THIOPHEN?
L73             QUE  ABB=ON  PLU=ON  "PYRIDAZINE DERIVATIVE"+PFT,OLD,NEW,
                NT/CT
L74             QUE  ABB=ON  PLU=ON  "PYRIDAZINONE DERIVATIVE"+PFT,OLD,NE
                W,NT/CT
L75             QUE  ABB=ON  PLU=ON  "THIAZOLE DERIVATIVE"+PFT,OLD,NEW,NT
                /CT
L76             QUE  ABB=ON  PLU=ON  "THIOPHENE DERIVATIVE"+PFT,OLD,NEW,N
                T/CT
L77         217 SEA FILE=EMBASE ABB=ON  PLU=ON  (L73 OR L74) AND ((L75 OR L76)
                OR L28)
L78             QUE  ABB=ON  PLU=ON  "PHOSPHODIESTERASE INHIBITOR"+PFT,OL
                D,NEW,NT/CT
L83          49 SEA FILE=EMBASE ABB=ON  PLU=ON  L27(5A)L28
L84           0 SEA FILE=EMBASE ABB=ON  PLU=ON  L83 AND L78
L85          14 SEA FILE=EMBASE ABB=ON  PLU=ON  L77 AND L83
L86           0 SEA FILE=EMBASE ABB=ON  PLU=ON  L83 AND L24
L87          14 SEA FILE=EMBASE ABB=ON  PLU=ON  (L84 OR L85 OR L86)


=> d his 192

     (FILE 'BIOSIS, PASCAL, JICST-EPLUS, JAPIO, LIFESCI, BIOENG, BIOTECHNO,
     BIOTECHDS, DRUGU, DRUGB, VETU, VETB, SCISEARCH, CONFSCI, DISSABS' ENTERED
     AT 12:26:38 ON 20 DEC 2006)
L92           1 S L91 AND L24

=> d que 192
L24             QUE  ABB=ON  PLU=ON  ?PHOSPHODIESTERAS? OR (?PHOSPHO(W)DI
                ESTERAS?) OR (?PHOSPHODI(W)ESTERAS?)
L27             QUE  ABB=ON  PLU=ON  ?PYRIDAZIN?
L28             QUE  ABB=ON  PLU=ON  ?THIAZOL? OR ?THIOPHEN?
L91         423 SEA L27(7A) L28
L92           1 SEA L91 AND L24


=> dup rem l35 l43 l46 l48 l51 l53 l58 l98 l71 l87 l92
DUPLICATE IS NOT AVAILABLE IN 'CHEMINFORMRX'.
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PROCESSING COMPLETED FOR L46
PROCESSING COMPLETED FOR L48
PROCESSING COMPLETED FOR L51
PROCESSING COMPLETED FOR L53
PROCESSING COMPLETED FOR L58
PROCESSING COMPLETED FOR L98
PROCESSING COMPLETED FOR L71
PROCESSING COMPLETED FOR L87
PROCESSING COMPLETED FOR L92
L99          69 DUP REM L35 L43 L46 L48 L51 L53 L58 L98 L71 L87...  (21 DUPLICATES
REMOVED)
                ANSWERS '1-32' FROM FILE HCAPLUS
                ANSWERS '33-34' FROM FILE USPATFULL
                ANSWER '35' FROM FILE TOXCENTER
                ANSWERS '36-37' FROM FILE CHEMINFORMRX
                ANSWERS '38-42' FROM FILE WPIX
                ANSWER '43' FROM FILE MARPAT
                ANSWERS '44-54' FROM FILE MEDLINE
                ANSWERS '55-68' FROM FILE EMBASE
                ANSWER '69' FROM FILE DRUGU
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=> file stnguide
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Dec 19, 2006 (20061219/UP).
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YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX,
WPIX, MEDLINE, EMBASE, DRUGU, MARPAT' - CONTINUE? (Y)/N:y


L99  ANSWER 1 OF 69  HCAPLUS  COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2006:886453  HCAPLUS  Full-text
DOCUMENT NUMBER:          145:292730
TITLE:                    Preparation of Naphthalene derivatives as modulators
                          of the glucocorticoid receptor
INVENTOR(S):              Rafferty, Stephen William; Turnbull, Philip Stewart;
                          Stewart, Eugene Lee; Caldwell, Richard Dana
PATENT ASSIGNEE(S):       Smithkline Beecham Corporation, USA
SOURCE:                   PCT Int. Appl., 249pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     --------------       ----   --------    --------------------     --------
     WO 2006091592         A1    20060831    WO 2006-US6096           20060221
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
             SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
             VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                        US 2005-655603P     P  20050223
OTHER SOURCE(S):          MARPAT 145:292730
ED   Entered STN:  31 Aug 2006
AB   Naphthalene derivs. I, wherein n is an integer from 1-4; R1 is cyano or nitro;
     Y is a carbonyl; Z is an alkylene or an (un)substituted alkylene ether; ; R2
     is alkyl, cyano, (un)substituted cycloalkyl, (un)substituted aryl,
     (un)substituted heteroaryl, etc; m and o are 0 or 1 are prepared for use in
     treating diseases related to that are modulation of the glucocorticoid
     receptor.  Thus, II was prepared and tested in a variety of biol. studies,
     including, but not limited to glucocorticoid, androgen and progesterone
     receptor fluorescence polarization assays; cellular tyrosine aminotransferase
     assay and an in vivo gluconeogenesis model on mice (no data).  Further, I can
     be used to treat ailments such as type 2 diabetes, type 1 diabetes,
     hyperglycemia, insulin resistance, metabolic syndrome X, diabetic
     dyslipidemia, bipolar disorder (manic depression), drug dependency, sleep
     disorders, schizophrenia, obsessive-compulsive disorder, post-traumatic stress
     disorder, social anxiety disorder, and generalized anxiety disorder.
CC   25-24 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
     Section cross-reference(s): 1, 27, 28, 63
IT   908267-47-0P   908267-50-5P   908267-53-8P   908267-56-1P   908267-59-4P
     908267-61-8P   908267-62-9P   908267-64-1P   908267-67-4P   908267-69-6P
     908267-71-0P   908267-73-2P   908267-75-4P   908267-77-6P   908267-79-8P
     908267-81-2P   908267-83-4P   908267-85-6P   908267-87-8P   908267-88-9P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of naphthalene derivs. as modulators of the glucocorticoid receptor)

IT 908272-48-0P 908272-49-1P 908272-50-4P 908272-51-5P 908272-52-6P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of naphthalene derivs. as modulators of the glucocorticoid receptor)

IT 60-12-8, 2-(Phenyl)ethanol 66-25-1, Hexanal 66-77-3, 1-Naphthalenecarboxaldehyde 66-99-9, 2-Naphthalenecarboxaldehyde 67-36-7 79-30-1, Isobutyryl chloride 89-75-8, 2,4-Dichlorobenzoyl chloride 89-98-5, 2-Chlorobenzaldehyde 93-25-4 93-40-3 95-48-7, o-Cresol, reactions 98-88-4, Benzoyl chloride 100-07-2 103-80-0, Phenylacetyl chloride 104-53-0, 3-Phenylpropanal 104-87-0, 4-Methylbenzaldehyde 104-88-1, 4-Chlorobenzaldehyde, reactions 104-97-2, Cyclopentanepropanoyl chloride 105-07-7, 4-Cyanobenzaldehyde 106-44-5, p-Cresol, reactions 108-12-3, 3-Methylbutanoyl chloride 108-43-0, 3-Chlorophenol 108-95-2, Phenol, reactions 109-64-8, 1,3-Dibromopropane 110-52-1, 1,4-Dibromobutane 111-24-0, 1,5-Dibromopentane 122-03-2, 4-(1-Methylethyl)benzaldehyde 123-11-5, reactions 135-02-4 141-75-3, Butanoyl chloride 312-94-7, 2-(Trifluoromethyl)benzoyl chloride 329-15-7, 4-(Trifluoromethyl)benzoyl chloride 351-35-9, [3-(Trifluoromethyl)phenyl]acetic acid 393-52-2, 2-Fluorobenzoyl chloride 401-95-6, 3,5-Bis(trifluoromethyl)benzaldehyde 405-50-5, (4-Fluorophenyl)acetic acid 446-52-6, 2-Fluorobenzaldehyde 447-61-0, 2-(Trifluoromethyl)benzaldehyde 451-82-1, (2-Fluorophenyl)acetic acid 454-89-7, 3-(Trifluoromethyl)benzaldehyde 455-01-6, 2-[3-(Trifluoromethyl)phenyl]ethanol 455-19-6, 4-(Trifluoromethyl)benzaldehyde 456-48-4, 3-Fluorobenzaldehyde 458-45-7, 3-(3-Fluorophenyl)propanoic acid 459-31-4, 3-(4-Fluorophenyl)propanoic acid 459-57-4, 4-Fluorobenzaldehyde 498-62-4, 3-**Thiophenecarboxaldehyde** 500-22-1, 3-Pyridinecarboxaldehyde 527-69-5, 2-Furancarbonyl chloride 529-20-4, 2-Methylbenzaldehyde 581-96-4, (2-Naphthalenyl)acetic acid 585-50-2 586-75-4, 4-Bromobenzoyl chloride 587-04-2, 3-Chlorobenzaldehyde 591-31-1 605-61-8, 1-Chloro-4-nitronaphthalene 606-83-7, 3,3-Diphenylpropanoic acid 613-45-6 620-02-0, 5-Methyl-2-furancarboxaldehyde 620-23-5, 3-Methylbenzaldehyde 621-36-3, (3-Methylphenyl)acetic acid 622-47-9, (4-Methylphenyl)acetic acid 638-29-9, Pentanoyl chloride 644-36-0, (2-Methylphenyl)acetic acid 645-45-4, Benzenepropanoyl chloride 653-21-4, (Pentafluorophenyl)acetic acid 659-28-9 699-02-5, 2-(4-Methylphenyl)ethanol 701-99-5,

(Phenyloxy)acetyl chloride 772-14-5, (3R)-3-Phenylbutanoic acid 773-99-9, 2-(1-Naphthalenyl)ethanol 872-85-5, 4-Pyridinecarboxaldehyde 874-60-2, 4-Methylbenzoyl chloride 879-18-5, 1-Naphthalenecarbonyl chloride 933-88-0, 2-Methylbenzoyl chloride 935-13-7, 2-Furanpropanoic acid 940-31-8 1074-16-4, 2-(2-Bromophenyl)ethanol 1121-60-4, 2-Pyridinecarboxaldehyde 1122-72-1, 6-Methyl-2-pyridinecarboxaldehyde 1122-91-4, 4-Bromobenzaldehyde 1122-99-2, Cyclopentylacetyl chloride 1200-14-2, 4-Butylbenzaldehyde 1505-50-6, 3-(4-Methylphenyl)propanoic acid 1643-26-1, 3-(2-Fluorophenyl)propanoic acid 1643-28-3, 3-(2-Chlorophenyl)propanoic acid 1643-30-7, 3-(4-Bromophenyl)propanoic acid 1710-98-1, 4-(1,1-Dimethylethyl)benzoyl chloride 1711-05-3 1711-06-4, 3-Methylbenzoyl chloride 1711-07-5, 3-Fluorobenzoyl chloride 1711-09-7, 3-Bromobenzoyl chloride 1711-11-1, 3-Cyanobenzoyl chloride 1798-09-0 1871-76-7, Diphenylacetyl chloride 1875-88-3, 2-(4-Chlorophenyl)ethanol 1875-89-4, 2-(3-Methylphenyl)ethanol 1877-73-2, (3-Nitrophenyl)acetic acid 1878-67-7, (3-Bromophenyl)acetic acid 1878-68-8, (4-Bromophenyl)acetic acid 1899-24-7, 5-Bromo-2-furancarboxaldehyde 1912-48-7, (1-Methyl-1H-indol-3-yl)acetic acid 1918-77-0, (2-Thienyl)acetic acid 1929-29-9 2043-61-0, Cyclohexanecarboxaldehyde 2243-83-6, 2-Naphthalenecarbonyl chloride 2251-65-2, 3-(Trifluoromethyl)benzoyl chloride 2719-27-9, Cyclohexanecarbonyl chloride 2745-26-8, (2-Furanyl)acetic acid 2815-95-4, 1,3-Benzodioxole-5-propanoic acid 2881-63-2 3034-50-2, 1H-Imidazole-4-carboxaldehyde 3038-48-0, [2-(Trifluoromethyl)phenyl]acetic acid 3132-99-8, 3-Bromobenzaldehyde 3249-68-1, Ethyl 3-oxohexanoate 3446-89-7, 4-(Methylthio)benzaldehyde 3457-45-2, 4-Acetylbenzaldehyde 3920-50-1, 1H-Pyrazole-3-carboxaldehyde 4023-34-1, Cyclopropanecarbonyl chloride 4315-07-5 4524-93-0, Cyclopentanecarbonyl chloride 4593-90-2, 3-Phenylbutanoic acid 4693-91-8 4701-17-1, 5-Bromo-2-**thiophenecarboxaldehyde** 4748-78-1, 4-Ethylbenzaldehyde 4919-33-9 4949-44-4, Ethyl 3-oxopentanoate 5006-22-4, Cyclobutanecarbonyl chloride 5020-41-7 5238-27-7, 2-Methylpentanoyl chloride 5271-67-0, 2-**Thiophenecarbonyl** chloride 5331-42-0 5398-77-6, 4-(Methylsulfonyl)benzaldehyde 5623-81-4, Cyclopentylacetaldehyde 5736-88-9 5779-95-3, 3,5-Dimethylbenzaldehyde 5807-30-7, (3,4-Dichlorophenyl)acetic acid 5834-16-2, 3-Methyl-2-**thiophenecarboxaldehyde** 6002-15-9, 1-Phenyl-1H-imidazole-2-carboxaldehyde 6068-72-0, 4-Cyanobenzoyl chloride 6287-38-3, 3,4-Dichlorobenzaldehyde 6342-77-4 6469-32-5 6630-33-7, 2-Bromobenzaldehyde 6654-36-0, Methyl 6-oxohexanoate 6834-42-0 6950-92-1 6964-21-2, (3-Thienyl)acetic acid 7065-46-5 7152-15-0, Ethyl 4-methyl-3-oxopentanoate 7154-66-7, 2-Bromobenzoyl chloride 7311-34-4 7468-67-9, 2-Cyanobenzaldehyde 7589-27-7, 2-(4-Fluorophenyl)ethanol 10031-82-0 10111-08-7, 1H-Imidazole-2-carboxaldehyde 10203-08-4, 3,5-Dichlorobenzaldehyde 10516-71-9 10551-58-3 13679-70-4, 5-Methyl-2-**thiophenecarboxaldehyde** 13750-81-7, 1-Methyl-1H-imidazole-2-carboxaldehyde 13794-14-4 13916-99-9, 4-Fluoro-1-naphthalenecarbonitrile 15115-58-9 16251-77-7, 3-Phenylbutanal 16340-68-4, 2,2,3,3-Tetramethylcyclopropanecarboxaldehyde 16681-68-8, 1H-1,2,3-Triazole-4-carboxaldehyde 18698-96-9, (2-Iodophenyl)acetic acid 18698-97-0, (2-Bromophenyl)acetic acid 18791-75-8, 4-Bromo-2-**thiophenecarboxaldehyde** 18791-79-2, 5-Bromo-3-**thiophenecarboxaldehyde** 19819-95-5, 2-(2-Chlorophenyl)ethanol 19819-98-8, 2-(2-Methylphenyl)ethanol 19955-99-8 21615-34-9 21640-48-2, 3-(3-Chlorophenyl)propanoic acid 22047-88-7 22084-89-5, 3-(2-Methylphenyl)propanoic acid 22545-15-9 22924-15-8 23074-10-4, 5-Ethyl-2-furancarboxaldehyde 24964-64-5, 3-Cyanobenzaldehyde 25016-09-5, 1,3-Dimethyl-1H-pyrazole-5-carboxaldehyde 25026-34-0, 4-(Chlorophenyl)acetyl chloride 25173-68-6,

3-(3,4-Dichlorophenyl)propanoic acid 25563-02-4 26033-20-5
26510-52-1, Ethyl 3-oxo-3-(2-pyridinyl)propanoate 27006-76-4,
5-Chloro-1,3-dimethyl-1H-pyrazole-4-carboxaldehyde 28229-69-8,
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Dichlorophenyl)ethanol 32085-88-4, 3,5-Difluorobenzaldehyde 32852-81-6
32857-62-8, [4-(Trifluoromethyl)phenyl]acetic acid 32863-32-4,
2,1,3-Benzoxadiazole-4-carboxaldehyde 33166-79-9 33224-99-6
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chloride 36878-91-8 37777-76-7, (2-Chloro-6-fluorophenyl)acetic acid
39515-51-0 42287-90-1, 3-(3-Bromophenyl)propanoic acid 51748-27-7,
3-[(Trifluoromethyl)thio]benzaldehyde 52022-77-2, 2-(3-
Nitrophenyl)ethanol 52059-53-7, 2-(3-Fluorophenyl)ethanol 52130-30-0,
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3-[4-(Trifluoromethyl)phenyl]propanoic acid 54221-96-4 54605-72-0
55116-09-1, 2-(Bromophenyl)acetyl chloride 56990-02-4,
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59664-42-5, 2,4-Bis(trifluoromethyl)benzaldehyde 59756-83-1 63131-29-3
65924-65-4, 2-[(1,1-Dimethylethyl)thio]benzaldehyde 68282-47-3,
2-Phenyl-1H-imidazole-4-carboxaldehyde 68282-49-5, 2-Butyl-1H-imidazole-
4-carboxaldehyde 68282-53-1, 4-Methyl-1H-imidazole-5-carboxaldehyde
69395-13-7, 2-(4-Cyanophenyl)ethanol 70201-43-3, 3-Bromo-4-
pyridinecarboxaldehyde 70289-12-2 70416-53-4 72775-83-8 78738-39-3
81156-68-5, 2-(2,4-Dichlorophenyl)ethanol 81228-09-3,
(2,4-Difluorophenyl)acetic acid 83902-00-5 85068-28-6,
(2,6-Difluorophenyl)acetic acid 86270-03-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of naphthalene derivs. as modulators of the glucocorticoid receptor)

IT 88634-80-4 89479-66-3, 3-Methyl-5-phenyl-4-isoxazolecarboxaldehyde
89990-54-5 90176-80-0, 4-Fluoro-2-(trifluoromethyl)benzaldehyde
93618-66-7 94022-96-5 94651-33-9 102191-92-4 112641-20-0,
2-Fluoro-3-(trifluoromethyl)benzaldehyde 128455-62-9,
5-Chloro-1-methyl-3-(trifluoromethyl)-1H-pyrazole-4-carboxaldehyde
132274-70-5, 1-Phenyl-1H-pyrazole-5-carboxaldehyde 132706-12-8,
5-(2-Pyridinyl)-2-**thiophenecarboxaldehyde** 145689-41-4,
(2,3-Difluorophenyl)acetic acid 146624-87-5 149806-06-4,
6-Bromo-3-pyridinecarboxaldehyde 161398-36-3 161712-75-0,
3-(3,4-Difluorophenyl)propanoic acid 162046-61-9 175136-79-5
177985-32-9, (2-Chloro-4-fluorophenyl)acetic acid 179946-32-8
181772-16-7 188815-30-7, 3-Fluoro-5-(trifluoromethyl)benzaldehyde
195044-13-4 195447-80-4 203302-97-0 212755-76-5 212755-77-6
214262-87-0 220239-67-8 252662-37-6 287917-97-9,
4-Bromo-1H-pyrazole-3-carboxaldehyde 350988-62-4 395090-68-3
886499-74-7 908268-45-1 908269-54-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of naphthalene derivs. as modulators of the glucocorticoid receptor)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Aventis Pharma Sa	2003			FR 2835835 A	HCAPLUS
Cadilla, R	2004			WO 2004110978 A	HCAPLUS

IT **908268-47-3P 908268-57-5P 908268-81-5P**
908268-83-7P 908269-16-9P 908269-36-3P
908272-54-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of naphthalene derivs. as modulators of the glucocorticoid receptor)

RN 908268-47-3 HCAPLUS
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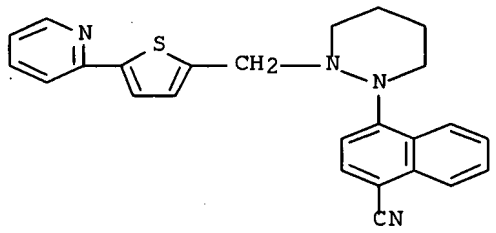
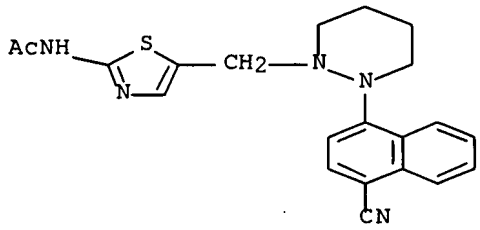


RN 908268-57-5 HCAPLUS
CN Acetamide, N-[5-[[2-(4-cyano-1-naphthalenyl)tetrahydro-1(2H)-pyridazinyl]methyl]-2-thiazolyl]- (9CI) (CA INDEX NAME)



RN 908268-81-5 HCAPLUS
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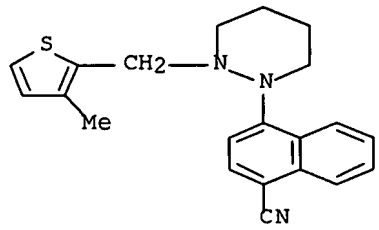

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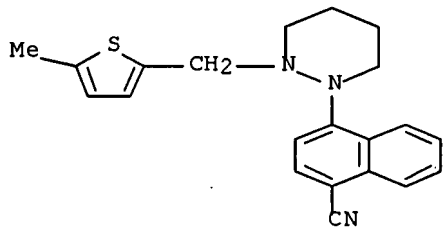

RN 908269-16-9 HCAPLUS
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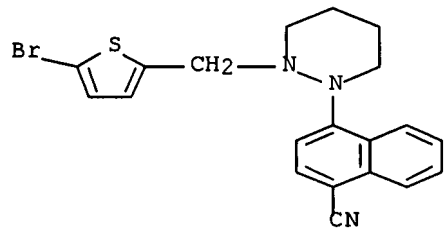
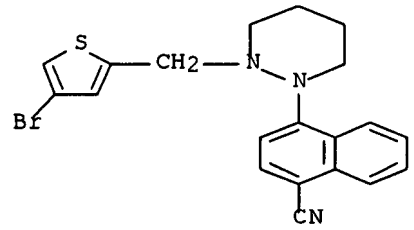
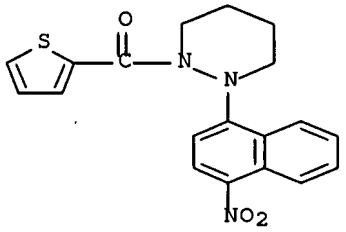


RN 908269-36-3 HCAPLUS
CN 1-Naphthalenecarbonitrile, 4-[2-[(4-bromo-2-thienyl)methyl]tetrahydro-1(2H)-pyridazinyl]- (9CI) (CA INDEX NAME)



RN 908272-54-8 HCAPLUS
CN Pyridazine, hexahydro-1-(4-nitro-1-naphthalenyl)-2-(2-thienylcarbonyl)- (9CI) (CA INDEX NAME)



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L99 ANSWER 2 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:2882 HCAPLUS Full-text
DOCUMENT NUMBER: 140:77154
TITLE: Preparation of **thiazoles** as **phosphodiesterase** IV inhibitors for the treatment of osteoporosis, tumors and cachexia
INVENTOR(S): Egggenweiler, Hans-Michael; Wolf, Michael
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000839	A1	20031231	WO 2003-EP4434	20030428 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2003232215	A1	20040106	AU 2003-232215	20030428 <--
BR 2003011879	A	20050315	BR 2003-11879	20030428 <--
EP 1513837	A1	20050316	EP 2003-760583	20030428 <--
EP 1513837	B1	20060830		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1662529	A	20050831	CN 2003-814060	20030428 <--
JP 2005530825	T	20051013	JP 2004-514623	20030428 <--
AT 338041	T	20060915	AT 2003-760583	20030428 <--

US 2005222160 A1 20051006 US 2004-518503 20041220 <--
PRIORITY APPLN. INFO.: DE 2002-10227269 A 20020619 <--
WO 2003-EP4434 W 20030428 <--

OTHER SOURCE(S): MARPAT 140:77154
ED Entered STN: 02 Jan 2004
AB Title compds. I [R1, R2 = H, OH, OR8, etc.; R8 = A, cycloalkyl, alkenyl, etc.; R3 = H, A"R7, COA"R7, etc.; A = alkyl, alkenyl; R7 = H, CO2H, CONH2, etc.; A" = alkylene, alkenylene, cycloalkylene, etc.; V, W = O, OH with the proviso that if V = O, then W = H, H; B = (un)substituted aromatic isocyclic, heterocyclic e.g., pyridyl, pyridyl-N- oxide, thienyl, etc.; X = N, CR3] their pharmaceutically acceptable salts and formulations were prepared For example, coupling of acid chloride II, e.g., prepared from 4-methyl-2-pyridin-2-**ylthiazole**-5-carboxylic acid Me ester in 3-steps, and 3-(3-cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H- **pyridazine** afforded claimed **thiazole** III. Compds. I are claimed useful as **phosphodiesterase** IV inhibitors (no data provided) for the treatment of osteoporosis, tumors, cachexia, etc.
IC ICM C07D417-14
ICS C07D417-06; A61K031-50; A61P011-06; A61P019-02; A61P019-10; A61P029-00; A61P035-00
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
ST osteoporosis prepn **phosphodiesterase** **thiazole** inhibition; tumor prepn **phosphodiesterase** **thiazole** inhibition; cachexia prepn **phosphodiesterase** **thiazole** inhibition
IT Inflammation
(Crohn's disease; preparation of **thiazoles** as **phosphodiesterase** IV inhibitors for the treatment of osteoporosis, tumors and cachexia)
IT Intestine, disease
(Crohn's; preparation of **thiazoles** as **phosphodiesterase** IV inhibitors for the treatment of osteoporosis, tumors and cachexia)
IT Dermatitis
(atopic; preparation of **thiazoles** as **phosphodiesterase** IV inhibitors for the treatment of osteoporosis, tumors and cachexia)
IT Bronchi, disease
Inflammation
(chronic bronchitis; preparation of **thiazoles** as **phosphodiesterase** IV inhibitors for the treatment of osteoporosis, tumors and cachexia)
IT Neoplasm
(metastasis; preparation of **thiazoles** as **phosphodiesterase** IV inhibitors for the treatment of osteoporosis, tumors and cachexia)
IT AIDS (disease)
Allergy
Allergy inhibitors
Anti-AIDS agents
Anti-inflammatory agents
Antiarteriosclerotics
Antiasthmatics
Antidiabetic agents
Antirheumatic agents
Antitumor agents
Arteriosclerosis
Asthma
Autoimmune disease
Cachexia
Cardiovascular agents
Diabetes mellitus
Heart, disease

Human
Inflammation
Multiple sclerosis
Neoplasm
Osteoporosis
Psoriasis
Rheumatoid arthritis
Sepsis
Skin, disease
(preparation of **thiazoles** as **phosphodiesterase** IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

IT Inflammation
Intestine, disease
(ulcerative colitis; preparation of **thiazoles** as **phosphodiesterase** IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

IT **640743-35-7P** **640743-36-8P** **640743-37-9P** **640743-38-0P**, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyridin-3-**ylthiazol**-5-yl)methanone **640743-39-1P**, 1-[3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyridin-3-**ylthiazol**-5-yl)methanone **640743-40-4P**, 1-[3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyridin-3-**ylthiazol**-5-yl)methanone **640743-41-5P**, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyridin-2-**ylthiazol**-5-yl)methanone **640743-42-6P**, 1-[3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyridin-2-**ylthiazol**-5-yl)methanone **640743-43-7P**, 1-[3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyridin-2-**ylthiazol**-5-yl)methanone **640743-44-8P**, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyrazin-2-**ylthiazol**-5-yl)methanone **640743-45-9P**, 1-[3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyrazin-2-**ylthiazol**-5-yl)methanone **640743-46-0P**, 1-[3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyrazin-2-**ylthiazol**-5-yl)methanone **640743-47-1P**, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-**thiophen**-2-**ylthiazol**-5-yl)methanone **640743-48-2P**, 1-[3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-**thiophen**-2-**ylthiazol**-5-yl)methanone **640743-49-3P**, 1-[3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-**thiophen**-2-**ylthiazol**-5-yl)methanone **640743-50-6P**, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-**phenylthiazol**-5-yl)methanone **640743-51-7P**, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-[4-methyl-2-(4-methoxyphenyl)**thiazol**-5-yl]methanone **640743-52-8P**, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-[4-methyl-2-(4-aminophenyl)**thiazol**-5-yl]methanone **640743-53-9P** **640743-54-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of **thiazoles** as **phosphodiesterase** IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

IT 640743-56-2P 640743-57-3P 640743-58-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of **thiazoles** as **phosphodiesterase** IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

IT 9036-21-9, **Phosphodiesterase** IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of **thiazoles** as **phosphodiesterase** IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

IT 109-77-3, Propanedinitrile 937-14-4 257876-11-2 438627-45-3, 3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazine** 640743-55-1, 4-Methyl-2-pyridin-2-**ylthiazole**-5-carboxylic acid methyl ester 640743-59-5, 3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazine** 640743-60-8, 3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazine** 640743-61-9 640743-62-0 640743-63-1 **640743-64-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **thiazoles** as **phosphodiesterase** IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

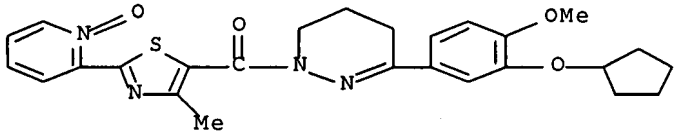
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Merck Patent Gmbh	1997			EP 0763534 A	HCAPLUS
Werner, K	1998			WO 9806704 A	HCAPLUS

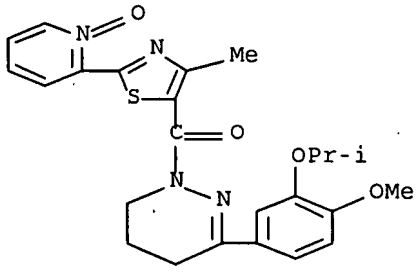
IT **640743-35-7P** **640743-36-8P** **640743-37-9P** **640743-38-0P**, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyridin-3-**ylthiazol**-5-yl)methanone **640743-39-1P**, 1-[3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyridin-3-**ylthiazol**-5-yl)methanone **640743-40-4P**, 1-[3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyridin-3-**ylthiazol**-5-yl)methanone **640743-41-5P**, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyridin-2-**ylthiazol**-5-yl)methanone **640743-42-6P**, 1-[3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyridin-2-**ylthiazol**-5-yl)methanone **640743-43-7P**, 1-[3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyridin-2-**ylthiazol**-5-yl)methanone **640743-44-8P**, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyrazin-2-**ylthiazol**-5-yl)methanone **640743-45-9P**, 1-[3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyrazin-2-**ylthiazol**-5-yl)methanone **640743-46-0P**, 1-[3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-pyrazin-2-**ylthiazol**-5-yl)methanone **640743-47-1P**, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-**thiophen**-2-**ylthiazol**-5-yl)methanone **640743-48-2P**, 1-[3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-**thiophen**-2-**ylthiazol**-5-yl)methanone **640743-49-3P**, 1-[3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-**thiophen**-2-**ylthiazol**-5-yl)methanone **640743-50-6P**, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-(4-methyl-2-**phenylthiazol**-5-yl)methanone **640743-51-7P**, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-**pyridazin**-1-yl]-1-[4-methyl-2-(4-methoxyphenyl)**thiazol**-5-yl]methanone **640743-52-8P**, 1-[3-(3-Ethoxy-4-methoxyphenyl)-

5,6-dihydro-4H-**pyridazin**-1-yl]-1-[4-methyl-2-(4-aminophenyl) **thiazol**-5-yl]methanone **640743-53-9P** **640743-54-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of **thiazoles** as **phosphodiesterase** IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

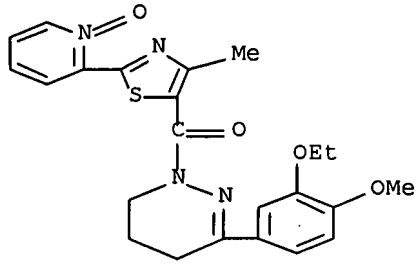
RN 640743-35-7 HCAPLUS
CN Pyridazine, 3-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,4,5,6-tetrahydro-1-[[4-methyl-2-(1-oxido-2-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



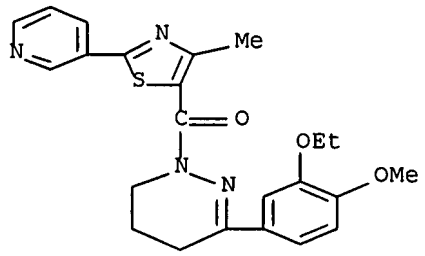
RN 640743-36-8 HCAPLUS
CN Pyridazine, 1,4,5,6-tetrahydro-3-[4-methoxy-3-(1-methylethoxy)phenyl]-1-[[4-methyl-2-(1-oxido-2-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



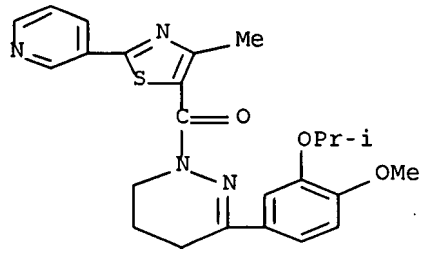
RN 640743-37-9 HCAPLUS
CN Pyridazine, 3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro-1-[[4-methyl-2-(1-oxido-2-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



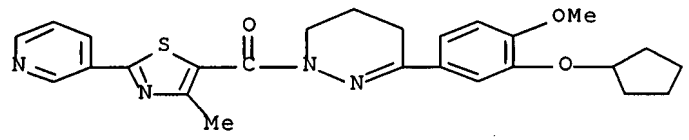
RN 640743-38-0 HCAPLUS
CN Pyridazine, 3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro-1-[[4-methyl-2-(3-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



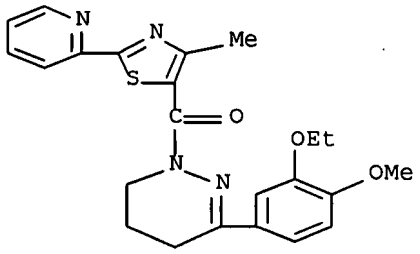
RN 640743-39-1 HCAPLUS
CN Pyridazine, 1,4,5,6-tetrahydro-3-[4-methoxy-3-(1-methylethoxy)phenyl]-1-[[4-methyl-2-(3-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



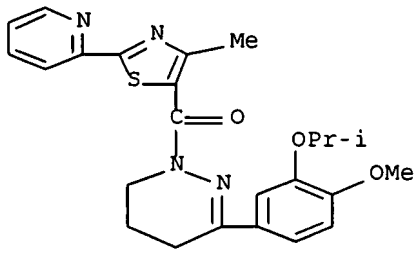
RN 640743-40-4 HCAPLUS
CN Pyridazine, 3-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,4,5,6-tetrahydro-1-[[4-methyl-2-(3-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



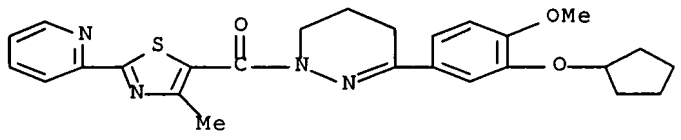
RN 640743-41-5 HCAPLUS
CN Pyridazine, 3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro-1-[[4-methyl-2-(2-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



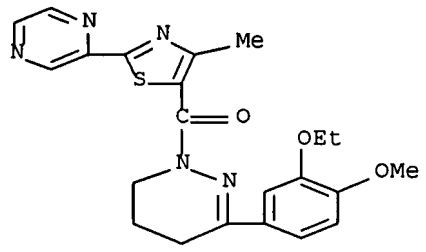
RN 640743-42-6 HCAPLUS
CN Pyridazine, 1,4,5,6-tetrahydro-3-[4-methoxy-3-(1-methylethoxy)phenyl]-1-[[4-methyl-2-(2-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



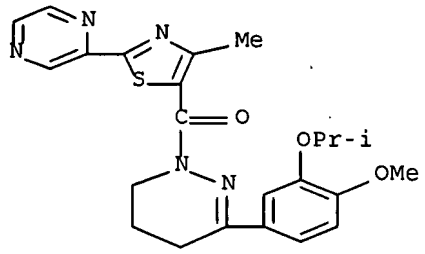
RN 640743-43-7 HCAPLUS
CN Pyridazine, 3-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,4,5,6-tetrahydro-1-[[4-methyl-2-(2-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



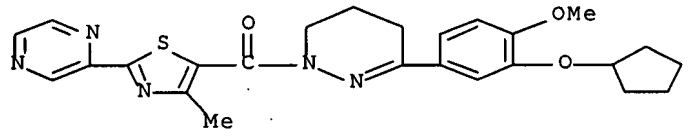
RN 640743-44-8 HCAPLUS
CN Pyridazine, 3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro-1-[(4-methyl-2-pyrazinyl-5-thiazolyl)carbonyl]- (9CI) (CA INDEX NAME)



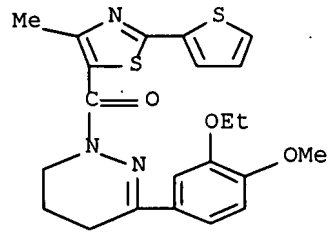
RN 640743-45-9 HCAPLUS
CN Pyridazine, 1,4,5,6-tetrahydro-3-[4-methoxy-3-(1-methylethoxy)phenyl]-1-[(4-methyl-2-pyrazinyl-5-thiazolyl)carbonyl]- (9CI) (CA INDEX NAME)



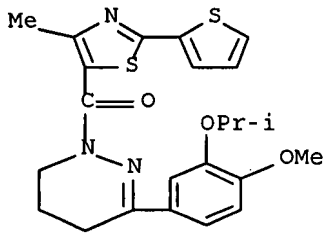
RN 640743-46-0 HCAPLUS
CN Pyridazine, 3-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,4,5,6-tetrahydro-1-[(4-methyl-2-pyrazinyl-5-thiazolyl)carbonyl]- (9CI) (CA INDEX NAME)



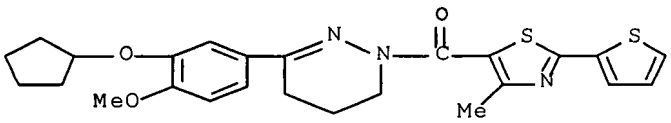
RN 640743-47-1 HCAPLUS
CN Pyridazine, 3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro-1-[[4-methyl-2-(2-thienyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



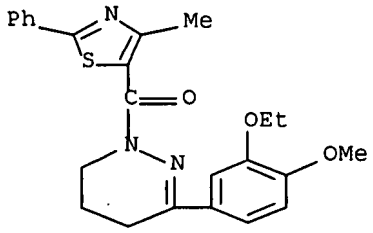
RN 640743-48-2 HCAPLUS
CN Pyridazine, 1,4,5,6-tetrahydro-3-[4-methoxy-3-(1-methylethoxy)phenyl]-1-[[4-methyl-2-(2-thienyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



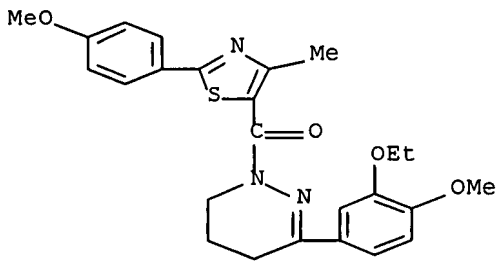
RN 640743-49-3 HCAPLUS
CN Pyridazine, 3-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,4,5,6-tetrahydro-1-[[4-methyl-2-(2-thienyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



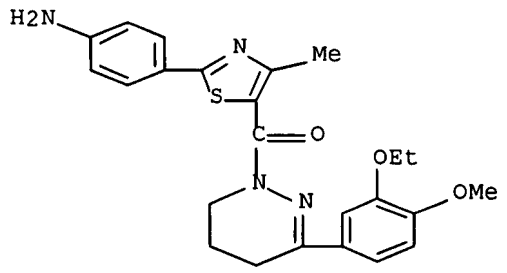
RN 640743-50-6 HCAPLUS
CN Pyridazine, 3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro-1-[(4-methyl-2-phenyl-5-thiazolyl)carbonyl]- (9CI) (CA INDEX NAME)



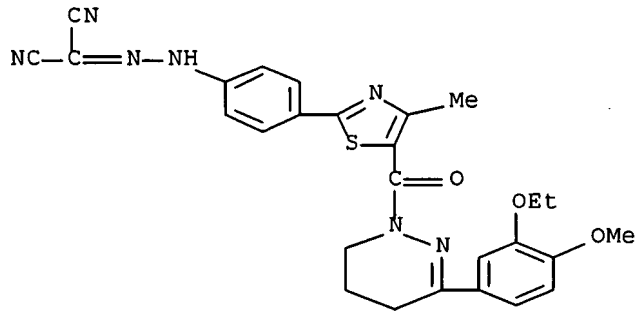
RN 640743-51-7 HCAPLUS
CN Pyridazine, 3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro-1-[[2-(4-methoxyphenyl)-4-methyl-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



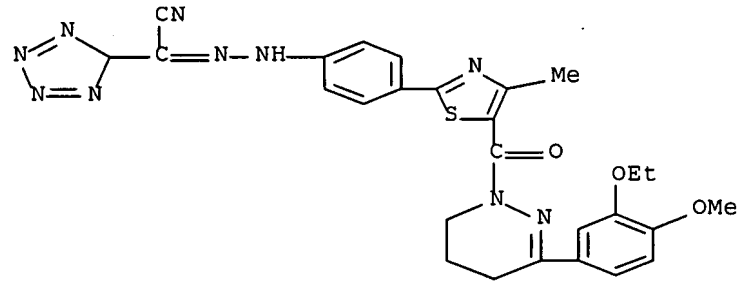
RN 640743-52-8 HCAPLUS
CN Pyridazine, 1-[[2-(4-aminophenyl)-4-methyl-5-thiazolyl]carbonyl]-3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro- (9CI) (CA INDEX NAME)



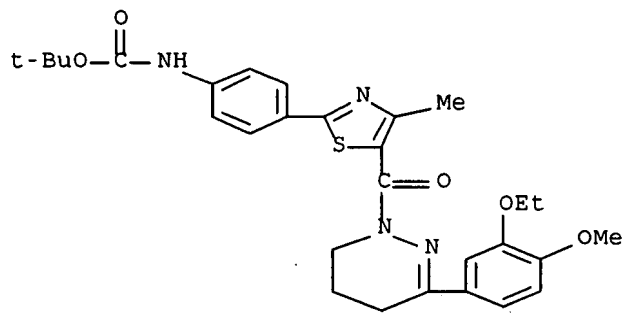
RN 640743-53-9 HCAPLUS
CN Pyridazine, 1-[[2-[4-[(dicyanomethylene)hydrazino]phenyl]-4-methyl-5-thiazolyl]carbonyl]-3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro- (9CI) (CA INDEX NAME)



RN 640743-54-0 HCAPLUS
CN Pyridazine, 1-[[2-[4-[(cyano-5H-tetrazol-5-ylmethylene)hydrazino]phenyl]-4-methyl-5-thiazolyl]carbonyl]-3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro- (9CI) (CA INDEX NAME)



IT **640743-64-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **thiazoles** as **phosphodiesterase** IV inhibitors for the treatment of osteoporosis, tumors and cachexia)
RN 640743-64-2 HCAPLUS
CN Carbamic acid, [4-[5-[[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-1(4H)-pyridazinyl]carbonyl]-4-methyl-2-thiazolyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L99 ANSWER 3 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2003:908829 HCAPLUS Full-text
DOCUMENT NUMBER: 140:94001
TITLE: Regioselective reduction of 2-(arylideneamino)isoindole-1,3-diones - synthesis of alkaloid analogues by N-acylhydrazonium ion aromatic π-cyclization
AUTHOR(S): Fogain-ninkam, Alain; Daich, Adam; Decroix, Bernard; Netchitailo, Pierre
CORPORATE SOURCE: URCOM, EA 3221, UFR des Sciences et Techniques, Universite du Havre, URCOM, EA 3221, UFR des Sciences et Techniques, Le Havre, 76058, Fr.
SOURCE: European Journal of Organic Chemistry (**2003**), (21), 4273-4278
CODEN: EJOCFK; ISSN: 1434-193X
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:94001
ED Entered STN: 20 Nov 2003
AB Hydroxylactams were synthesized by successive regioselective redns. of [(arylmethylene)amino]phthalimides, which were easily available from aminophthalimide and benzaldehyde of **thiophenecarboxaldehydes.** N-Acylhydrazonium ions, generated in the presence of Lewis acid from acetoxy derivs. of hydroxylactams, or in organic acid medium directly from hydroxylactams, induced the expected isoindolophthalazines and **thienopyridazinoisoindolones.** On the other hand, hydroxylactams under acidic conditions gave unexpected N-thienylmethyl-substituted **thienopyridazinoisoindolones.**
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 27, 31
ST isoindolophthalazinone prepn; **thienopyridazinoisoindolone** prepn; regioselective redn arylimino phthalimide; cyclization regioselective redn

arylimino phthalimide; alkaloid analog prepn cyclization regioselective redn arylimino phthalimide

IT 98-03-3, 2-**Thiophenecarboxaldehyde** 100-52-7, Benzaldehyde, reactions 498-62-4, 3-**Thiophenecarboxaldehyde** 1875-48-5, 2-Amino-1H-isoindole-1,3(2H)-dione
RL: RCT (Reactant); RACT (Reactant or reagent)
(regioselective reduction of (arylideneamino)isoindolediones and preparation of
alkaloid analogs by N-acylhydrazonium ion aromatic π-cyclization)

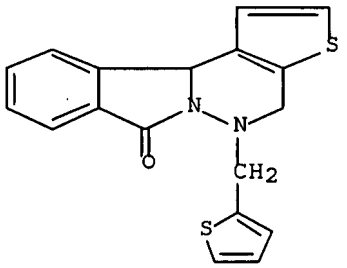
IT 643752-20-9P 643752-22-1P 643752-24-3P 643752-26-5P
643752-27-6P 643752-29-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(regioselective reduction of (arylideneamino)isoindolediones and preparation of
alkaloid analogs by N-acylhydrazonium ion aromatic π-cyclization)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Bartovic, A	2000	37	827	J Heterocyclic Chem	HCAPLUS
Bartovic, A	2000	37	827	J Heterocyclic Chem	HCAPLUS
Borch, R	1971	93	2897	J Am Chem Soc	HCAPLUS
Denmark, S	1988	53	1251	J Org Chem	HCAPLUS
Dhimane, H	1998		1955	Eur J Org Chem	HCAPLUS
Dudley, T	1999	64	1247	J Org Chem	HCAPLUS
Hiemstra, H	1991	2	1047	Comprehensive Organi	
Korenova, A	1998	35	9	J Heterocyclic Chem	HCAPLUS
Metais, E	1997	62	9210	J Org Chem	HCAPLUS
Nelsen, S	1973	14	2321	Tetrahedron Lett	
Othman, M	2000	52	273	Heterocycles	HCAPLUS
Pestellini, V	1978	13	296	Eur J Med Chem	HCAPLUS
Pigeon, P	1998	54	1497	Tetrahedron	HCAPLUS
Pigeon, P	1997	38	1041	Tetrahedron Lett	HCAPLUS
Rutjes, F	1993	49	10027	Tetrahedron	HCAPLUS
Rutjes, F	1993	49	8605	Tetrahedron	HCAPLUS
Rutjes, F	1988	29	6975	Tetrahedron Lett	HCAPLUS
Speckamp, W	2000	56	3817	Tetrahedron	HCAPLUS
Suzuki, H	1995	60	6114	J Org Chem	HCAPLUS
Teerhuis, N	1997	38	155	Tetrahedron Lett	HCAPLUS
Teerhuis, N	1997	38	159	Tetrahedron Lett	HCAPLUS

IT **643752-27-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(regioselective reduction of (arylideneamino)isoindolediones and preparation of
alkaloid analogs by N-acylhydrazonium ion aromatic π-cyclization)

RN 643752-27-6 HCAPLUS
CN Thieno[2',3':4,5]pyridazino[6,1-a]isoindol-7(5H)-one, 4,11b-dihydro-5-(2-thienylmethyl)- (9CI) (CA INDEX NAME)



L99 ANSWER 4 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2003:189365 HCAPLUS Full-text
DOCUMENT NUMBER: 139:78424
TITLE: **Pyridazinones** as selective cyclooxygenase-2 inhibitors
AUTHOR(S): Li, Chun Sing; Brideau, Christine; Chan, Chi Chung; Savoie, Chantal; Claveau, David; Charleson, Stella; Gordon, Robert; Greig, Gillian; Gauthier, Jacques Yves; Lau, Cheuk K.; Riendeau, Denis; Therien, Michel; Wong, Elizabeth; Prasit, Petpiboon
CORPORATE SOURCE: Merck Frosst Centre for Therapeutic Research, Pointe-Claire-Dorval, QC, 1005, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (**2003**), 13(4), 597-600
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:78424
ED Entered STN: 11 Mar 2003
AB **Pyridazinone** was found to be an excellent core template for selective COX-2 inhibitors. Two potent, selective and orally active COX-2 inhibitors (I and II), which were highly efficacious in rat paw edema and rat pyresis models, have been obtained.
CC 1-3 (Pharmacology)
Section cross-reference(s): 28
ST **pyridazinone** analog prepn cyclooxygenase 2 inhibitor antiinflammatory
IT Structure-activity relationship
(enzyme-inhibiting; preparation of **pyridazinones** as selective cyclooxygenase-2 inhibitors)
IT Anti-inflammatory agents
(preparation of **pyridazinones** as selective cyclooxygenase-2 inhibitors)
IT 329900-75-6, Cyclooxygenase-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of **pyridazinones** as selective cyclooxygenase-2 inhibitors)
IT 213763-79-2P 213763-80-5P 213763-81-6P 213763-82-7P 213763-83-8P
213763-92-9P 213763-96-3P 213763-99-6P 213764-00-2P 213764-01-3P
213764-05-7P 213764-08-0P 213764-13-7P 213764-14-8P
213764-15-9P 221025-57-6P 552865-16-4P 552865-17-5P 552865-18-6P
552865-19-7P 552865-20-0P 552865-21-1P 552865-22-2P 552865-23-3P
552865-24-4P 552865-25-5P 552865-26-6P 552865-27-7P 552865-28-8P
552865-29-9P

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **pyridazinones** as selective cyclooxygenase-2 inhibitors)

IT 67-63-0, 2-Propanol, reactions 74-83-9, Methane, bromo-, reactions 100-39-0, Benzene, (bromomethyl)- 108-86-1, Benzene, bromo-, reactions 108-98-5, **Thiophenol**, reactions 371-41-5, Phenol, 4-fluoro- 507-19-7, Propane, 2-bromo-2-methyl- 870-63-3, 2-Butene, 1-bromo-3-methyl- 2516-33-8, Cyclopropanemethanol 2550-36-9, Cyclohexane, (bromomethyl)- 4214-79-3 4333-56-6, Cyclopropane, bromo- 5042-30-8, Hydrazine, (2,2,2-trifluoroethyl)- 5720-05-8, Boronic acid, (4-methylphenyl)- 7051-34-5, Cyclopropane, (bromomethyl)- 36982-56-6, Cyclopropane, (2-bromoethyl)- 42082-19-9, Cyclopropane, 1-(bromomethyl)-1-methyl- 45438-73-1, **Thiophene**, 2-(bromomethyl)- 51598-33-5 51598-64-2 56634-50-5 69966-55-8, Pyridine, 3-(bromomethyl)- 80204-20-2 98546-51-1, Boronic acid, (4-**methylthiophenyl**)- 131654-56-3, **Thiazole**, 2-(bromomethyl)- 157672-00-9 162011-90-7 210117-20-7, Cyclopropane, 2-(bromomethyl)-1,1-dimethyl- 313272-18-3 659742-17-3 659742-21-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **pyridazinones** as selective cyclooxygenase-2 inhibitors)

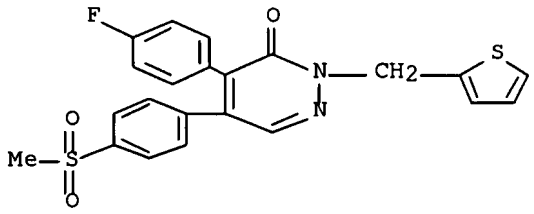
IT 162012-28-4P 185147-17-5P 213764-20-6P 213764-23-9P 552865-13-1P 552865-14-2P 552865-15-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of **pyridazinones** as selective cyclooxygenase-2 inhibitors)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Bombardier, C	2002	89	3-D	Am J Cardiol	
Brideau, C	1996	45	68	Inflamm Res	HCAPLUS
Chan, C	1995	274	1531	J Pharmacol Exp Ther	HCAPLUS
Charette, A	1995	60	1081	J Org Chem	HCAPLUS
Dannhardt, G	2001	36	109	Eur J Med Chem	HCAPLUS
Friesen, R	1998	8	2777	Bioorg Med Chem Lett	HCAPLUS
Jas, G	1991	11	965	Synthesis	
Kargman, S	1996	52	1113	Biochem Pharmacol	HCAPLUS
Li, J	1996	39	1846	J Med Chem	HCAPLUS
Penning, T	1997	40	1347	J Med Chem	HCAPLUS
Pinto, D	1999	9	919	Bioorg Med Chem Lett	HCAPLUS
Prasit, P	1999	9	1773	Bioorg Med Chem Lett	HCAPLUS
Riendeau, D	1997	75	1088	Can J Phys Pharmacol	HCAPLUS
Talley, J	2000	43	775	J Med Chem	HCAPLUS

IT **213764-05-7P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **pyridazinones** as selective cyclooxygenase-2 inhibitors)

RN 213764-05-7 HCAPLUS
CN 3(2H)-Pyridazinone, 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-2-(2-thienylmethyl)- (9CI) (CA INDEX NAME)

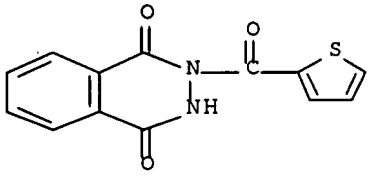


L99 ANSWER 5 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2002:106302 HCAPLUS Full-text
DOCUMENT NUMBER: 136:294791
TITLE: Reaction of 1,4-Phthalazinedione with Furfural: Formation of the [5,6]Benza-3a,7a-diazaindane System via an Unusual Skeletal Rearrangement
AUTHOR(S): Amarasekara, Ananda S.; Chandrasekara, Susantha
CORPORATE SOURCE: Department of Chemistry, University of Colombo, Colombo, Sri Lanka
SOURCE: Organic Letters (**2002**), 4(5), 773-775
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:294791
ED Entered STN: 10 Feb 2002
AB Oxidation of phthalhydrazide with lead tetraacetate in the presence of furfural or 5-methylfurfural in CH3Cl3 gave the carboxydiazabenzindenediones I (R = H, Me) in 64% and 46% yields, resp. Similar reaction of phthalhydrazide with 2-**thiophenecarboxaldehyde** gave the (thienylcarbonyl)phthalhydrazide II.
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
ST rearrangement oxidn cyclocondensation phthalhydrazide furfural; thienylcarbonylphthalhydrazide prepn; **thiophenecarboxaldehyde** oxidn cyclocondensation phthalhydrazide; benzdiazaindanedione carboxy prepn; phthalhydrazide lead tetraacetate oxidn cyclocondensation furfural
IT 98-03-3, 2-**Thiophenecarboxaldehyde**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (thienylcarbonyl)phthalhydrazide by oxidation/condensation of
thiophenecarboxaldehyde with phthalhydrazide)
IT **408535-41-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of (thienylcarbonyl)phthalhydrazide by oxidation/condensation of
thiophenecarboxaldehyde with phthalhydrazide)
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Agmon, I	1986	108	4477	J Am Chem Soc	HCAPLUS
Alder, K	1954	81	585	Ann	
Amarasekara, A	2000	73	267	Bull Chem Soc Jpn	
Baldwin, J	1976		734	J Chem Soc, Chem Com	HCAPLUS
Baldwin, J	1976		736	J Chem Soc, Chem Com	HCAPLUS
Clement, R	1960	27	1115	J Org Chem	
Clement, R	1960	25	1724	J Org Chem	HCAPLUS
Cocharan, J	1996	37	2903	Tetrahedron Lett	

Cookson, R	1962		615	Tetrahedron Lett	HCAPLUS
Cramer, R	1960	79	6215	J Am Chem Soc	
Criegee, R	1965		311	Oxidation in Organic	
Dean, F	1982	31	237	Adv Heterocycl Chem	HCAPLUS
Filer, C	1979	44	285	J Org Chem	HCAPLUS
Friedrich, E	1975	40	720	J Org Chem	HCAPLUS
Johnson, C	1993	26	476	Acc Chem Res	HCAPLUS
Junculev, J	1961	33	59	Croat Chem Acta	
Kealy, T	1962	84	966	J Am Chem Soc	HCAPLUS
Lambert, J	1980	102	3588	J Am Chem Soc	HCAPLUS
Mavoungou-Gomes, L	1967		1764	Bull Soc Chim Fr	HCAPLUS
McClelland, R	1981	46	4345	J Am Chem Soc	HCAPLUS
Sternhell, S	1969	23	236	Q Rev	HCAPLUS
Wong, H	1983	20	1815	Heterocycles	HCAPLUS
Wong, H	1984	22	875	Heterocycles	HCAPLUS
Zaballos-Garcia, E	1997	53	9313	Tetrahedron	HCAPLUS

IT **408535-41-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of (thienylcarbonyl)phthalhydrazide by oxidation/condensation of
thiophenecarboxaldehyde with phthalhydrazide)
RN 408535-41-1 HCAPLUS
CN 1,4-Phthalazinedione, 2,3-dihydro-2-(2-thienylcarbonyl)- (9CI) (CA INDEX NAME)



L99 ANSWER 6 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2001:489398 HCAPLUS Full-text
DOCUMENT NUMBER: 135:92643
TITLE: Preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain
INVENTOR(S): Murphy, Megan; Urbanek, Rebecca Ann; Xiao, Wenhua; Steelman, Gary Banks; Brown, Dean Gordon; Bare, Thomas Michael
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047925	A1	20010705	WO 2000-SE2609	20001219 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,

LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001025662	A5	20010709	AU 2001-25662	20001219	<--
EP 1244664	A1	20021002	EP 2000-989117	20001219	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003519147	T	20030617	JP 2001-549395	20001219	<--
EP 1577311	A1	20050921	EP 2005-5708	20001219	<--
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ZA 2002004779	A	20030915	ZA 2002-4779	20020613	<--
ZA 2002004781	A	20030915	ZA 2002-4781	20020613	<--
US 2003153572	A1	20030814	US 2003-168762	20030212	<--
US 6730675	B2	20040504			

PRIORITY APPLN. INFO.:	US 1999-171906P	P	19991223 <--
	US 2000-236786P	P	20000929 <--
	US 2000-236783P	P	20000929 <--
	EP 2000-987935	A3	20001219 <--
	WO 2000-SE2609	W	20001219 <--

OTHER SOURCE(S): MARPAT 135:92643
ED Entered STN: 06 Jul 2001
AB The title compds. [I; R1 = halo; A = (CH2)n (n = 1-4); D = (un)substituted 5-membered heteroaryl or its benz- derivative], useful for treating pain, were prepared E.g., a multi-step synthesis of I [R1 = 7-Cl; A = CH2; D = 2,5-dimethylfuran-3-yl] which showed Ki of 24.8 nM in test for binding to NMDA receptor glycine site, was given.
IC ICM C07D471-04
ICS A61K031-5025
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
ST **pyridazinoquinolinedione** prepn analgesic NMDA receptor glycine site
IT Glutamate receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(NMDA-binding, glycine site; preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)
IT Analgesics
(preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)
IT 348088-73-3P **348088-74-4P** 348088-75-5P 348088-76-6P 348088-77-7P 348088-78-8P 348088-79-9P 348088-80-2P **348088-81-3P** **348088-82-4P** **348088-83-5P** 348088-84-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)
IT 123-75-1, Pyrrolidine, reactions 620-02-0, 5-Methylfurfural 762-42-5, Dimethyl acetylenedicarboxylate 870-46-2, tert-Butylcarbazate 5834-16-2, 3-**Methylthiophene**-2-carboxaldehyde 5900-58-3, Methyl 2-amino-4-chlorobenzoate 5904-71-2, Methyl 5-formylfuran-2-carboxylate 6141-58-8, Methyl 2-methyl-3-furoate 6148-34-1 13679-70-4, 5-**Methylthiophene**-2-carboxaldehyde 19788-37-5,

4-(Chloromethyl)-3,5-dimethylisoxazole 22053-74-3, 3-**Methylbenzothiophene**-2-carboxaldehyde 24006-09-5 30153-47-0 34035-04-6 52480-43-0 348088-91-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)

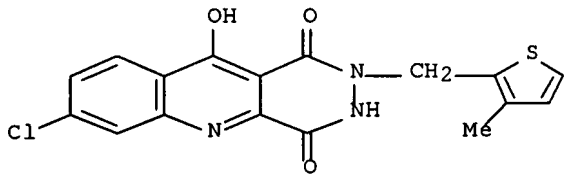
IT 1003-96-9P 113874-61-6P 147494-01-7P 170143-35-8P 179543-91-0P 179543-97-6P 348088-85-7P 348088-86-8P 348088-87-9P 348088-88-0P 348088-89-1P 348088-90-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)

RETABLE

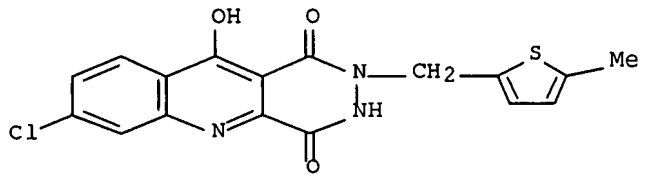
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Zeneca Limited	1995			WO 9511244 A1	HCAPLUS
Zeneca Limited	1996			EP 0736531 A1	HCAPLUS

IT **348088-74-4P 348088-81-3P 348088-82-4P 348088-83-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)

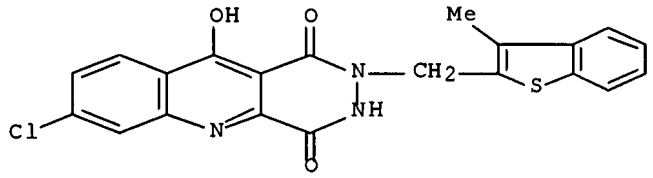
RN 348088-74-4 HCAPLUS
CN Pyridazino[4,5-b]quinoline-1,4-dione, 7-chloro-2,3-dihydro-10-hydroxy-2-[(3-methyl-2-thienyl)methyl]- (9CI) (CA INDEX NAME)



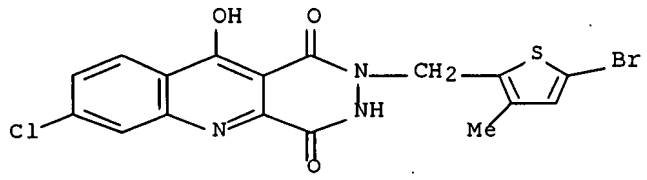
RN 348088-81-3 HCAPLUS
CN Pyridazino[4,5-b]quinoline-1,4-dione, 7-chloro-2,3-dihydro-10-hydroxy-2-[(5-methyl-2-thienyl)methyl]- (9CI) (CA INDEX NAME)



RN 348088-82-4 HCAPLUS
CN Pyridazino[4,5-b]quinoline-1,4-dione, 7-chloro-2,3-dihydro-10-hydroxy-2-[(3-methylbenzo[b]thien-2-yl)methyl]- (9CI) (CA INDEX NAME)



RN 348088-83-5 HCAPLUS
CN Pyridazino[4,5-b]quinoline-1,4-dione, 2-[(5-bromo-3-methyl-2-thienyl)methyl]-7-chloro-2,3-dihydro-10-hydroxy- (9CI) (CA INDEX NAME)



L99 ANSWER 7 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 2001:489232 HCAPLUS Full-text
DOCUMENT NUMBER: 135:92648
TITLE: Preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain
INVENTOR(S): Alford, Vernon; Bare, Thomas Michael; Brown, Dean Gordon; McLaren, Frances Marie; Murphy, Megan; Urbanek, Rebecca Ann; Xiao, Wenhua
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047523	A1	20010705	WO 2000-SE2605	20001219 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2394561	A1	20010705	CA 2000-2394561	20001219 <--
AU 2001025660	A5	20010709	AU 2001-25660	20001219 <--
AU 783499	B2	20051103		

BR 2000016646	A	20021008	BR 2000-16646		20001219 <--
EP 1248621	A1	20021016	EP 2000-989115		20001219 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
HU 200300043	A2	20030528	HU 2003-43		20001219 <--
JP 2003518499	T	20030610	JP 2001-548117		20001219 <--
EE 200200348	A	20030815	EE 2002-348		20001219 <--
NZ 519389	A	20040528	NZ 2000-519389		20001219 <--
RU 2238094	C2	20041020	RU 2002-115273		20001219 <--
EP 1577311	A1	20050921	EP 2005-5708		20001219 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
CZ 296493	B6	20060315	CZ 2002-2176		20001219 <--
ZA 2002004779	A	20030915	ZA 2002-4779		20020613 <--
ZA 2002004781	A	20030915	ZA 2002-4781		20020613 <--
BG 106832	A	20030331	BG 2002-106832		20020618 <--
NO 2002002990	A	20020820	NO 2002-2990		20020620 <--
US 2003162783	A1	20030828	US 2003-168745		20030128 <--
PRIORITY APPLN. INFO.:			US 1999-171906P	P	19991223 <--
			US 2000-236835P	P	20000929 <--
			US 2000-236783P	P	20000929 <--
			EP 2000-987935	A3	20001219 <--
			WO 2000-SE2605	W	20001219 <--

OTHER SOURCE(S): MARPAT 135:92648

ED Entered STN: 06 Jul 2001

AB The title compds. [I; A = (CH2)n (wherein n = 0-4); D = 5-6 membered heteroaryl or its benz- derivative having 1-3 ring atoms selected from O, N or S; R1 = halo], useful for the treatment of pain, were prepared E.g., a multi-step synthesis of I.MeSO3H [A = CH2; n = 1; D = 4-pyridyl; R1 = 7-Cl] which showed a Ki of 79 nM in a test for binding to the NMDA receptor glycine site, was given.

IC ICM A61K031-5025

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST **pyridazinoquinolinedione** prepn analgesic NMDA receptor glycine site

IT Glutamate receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(NMDA-binding, glycine site; preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)

IT Analgesics
(preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)

IT **170142-52-6P** 170143-15-4P 170143-16-5P 170143-17-6P
348627-82-7P 348627-83-8P 348627-84-9P 348627-85-0P 348627-87-2P
348627-88-3P 348627-90-7P 348627-91-8P 348627-93-0P 348627-95-2P
348627-96-3P 348627-98-5P 348627-99-6P **348628-04-6P**
348628-05-7P 348628-06-8P 348628-07-9P 348628-08-0P 348628-09-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)

IT 95-15-8, **Benzothiophene** 98-01-1, 2-Furaldehyde, reactions
98-03-3, **Thiophene**-2-carboxaldehyde 109-08-0, 2-Methylpyrazine
123-75-1, Pyrrolidine, reactions 498-60-2, 3-Furaldehyde 498-62-4, **Thiophene**-3-carboxaldehyde 762-42-5, Dimethyl acetylenedicarboxylate 870-46-2, tert-Butyl carbazate 1822-51-1,

4-Picolyl chloride hydrochloride 4265-16-1, Benzofuran-2-carboxaldehyde 4363-93-3, Quinoline-4-carboxaldehyde 5900-58-3, Methyl 2-amino-4-chlorobenzoate 6959-47-3, 2-Picolyl chloride hydrochloride 6959-48-4, 3-Picolyl chloride hydrochloride 10111-08-7, 2-Imidazolecarboxaldehyde 10200-59-6, 2-**Thiazolecarboxaldehyde** 54198-81-1, 4-Chloromethylpyrimidine 69735-35-9, 5-Bromomethylisoxazole
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)

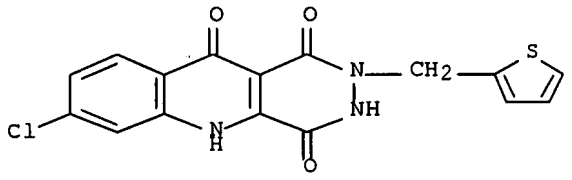
IT 3541-37-5P, Benzo[b]**thiophene**-2-carboxaldehyde 39204-47-2P, 2-Chloromethylpyrazine 113906-60-8P 147494-01-7P 150767-01-4P 150767-03-6P 150767-04-7P 162739-66-4P 162739-74-4P 162739-88-0P 170143-35-8P 182887-52-1P 182887-56-5P 348628-12-6P 348628-13-7P 348628-14-8P 348628-15-9P 348628-16-0P 348628-17-1P 348628-18-2P 348628-19-3P 348628-20-6P 348628-21-7P 348628-22-8P 348628-23-9P 348628-24-0P 348628-25-1P 348628-26-2P 348628-27-3P 348628-28-4P 348628-29-5P 348628-30-8P 348628-31-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)

RETABLE

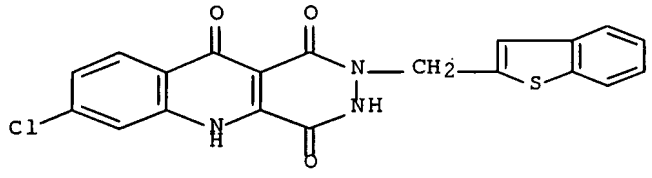
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Zeneca Limited	1995			WO 9511244 A1	HCAPLUS

IT **170142-52-6P 348628-04-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)

RN 170142-52-6 HCAPLUS
CN Pyridazino[4,5-b]quinoline-1,4,10(5H)-trione, 7-chloro-2,3-dihydro-2-(2-thienylmethyl)- (9CI) (CA INDEX NAME)



RN 348628-04-6 HCAPLUS
CN Pyridazino[4,5-b]quinoline-1,4,10(5H)-trione, 2-(benzo[b]thien-2-ylmethyl)-7-chloro-2,3-dihydro- (9CI) (CA INDEX NAME)



L99 ANSWER 8 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 2000:291005 HCAPLUS Full-text
DOCUMENT NUMBER: 132:321867
TITLE: Preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors
INVENTOR(S): Black, Lawrence A.; Basha, Anwer; Kolasa, Teodozyj; Kort, Michael E.; Liu, Huaqing; Mccarty, Catherine M.; Patel, Meena V.; Rohde, Jeffrey J.; Coghlan, Michael J.; Stewart, Andrew O.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 477 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000024719	A1	20000504	WO 1999-US25234		19991027 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2347982	A1	20000504	CA 1999-2347982		19991027 <--
AU 9965230	A1	20000515	AU 1999-65230		19991027 <--
AU 773237	B2	20040520			
EP 1124804	A1	20010822	EP 1999-953259		19991027 <--
EP 1124804	B1	20050824			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
US 6307047	B1	20011023	US 1999-427768		19991027 <--
BR 9914858	A	20020205	BR 1999-14858		19991027 <--
JP 2003512292	T	20030402	JP 2000-578289		19991027 <--
AT 302759	T	20050915	AT 1999-953259		19991027 <--
ZA 2001003310	A	20020723	ZA 2001-3310		20010423 <--
NO 2001002061	A	20010627	NO 2001-2061		20010426 <--
NO 318623	B1	20050418			
BG 105523	A	20011231	BG 2001-105523		20010519 <--
HK 1041876	A1	20060623	HK 2002-101207		20020219 <--
PRIORITY APPLN. INFO.:			US 1998-179605	A	19981027 <--
			US 1999-261872	A	19990303 <--
			US 1999-298490	A	19990423 <--
			US 1999-427768	A	19991027 <--
			US 1997-56733P	P	19970822 <--
			US 1998-129570	B2	19980805 <--
			US 1998-137457	B2	19980820 <--
			WO 1999-US25234	W	19991027 <--

OTHER SOURCE(S): MARPAT 132:321867
ED Entered STN: 05 May 2000

AB The title compds. [I; X = O, S, NR4, etc.; R4 = alkyl, alkenyl, cycloalkyl, etc.; R = H, alkyl, alkenyl, etc.; at least one of R1-R3 = II-III (wherein X1 = SO2, SO(NR10), SO, etc.; R9 = alkyl, alkenyl, alkynyl, etc.; X2 = H, halo, alkyl, etc.; R10 = H, alkyl, cycloalkyl); the remaining two of the groups of R1-R3 = H, OH, hydroxyalkyl, etc.] which are cyclooxygenase (COX) inhibitors, and in particular, are selective inhibitors of cyclooxygenase-2 (COX-2), and therefore are useful in treating pain, fever, inflammation, rheumatoid arthritis, osteoarthritis, adhesions, and cancer, were prepared Thus, oxidation of 2-benzyl-4-(4- fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-**pyridazinone** (preparation given) with MeCO3H in CH2Cl2 afforded 86% I [X = O; R = PhCH2; R1 = 4-FC6H4; R2 = 4-(MeSO2)C6H4; R3 = H], which showed 0.014 μM against COX-2. COX-2 is the inducible isoform associated with inflammation, as opposed to the constitutive isoform, cyclooxygenase-1 (COX-1) which is an important "housekeeping" enzyme in many tissues, including the gastrointestinal (GI) tract and the kidneys. The selectivity of the compds. I for COX-2 minimizes the unwanted GI and renal side-effects seen with currently marketed non-steroidal anti-inflammatory drugs (NSAIDs).

IC ICM C07D237-14
ICS A61K031-50; C07D405-04; C07D409-04

CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST prostaglandin endoperoxide H synthase biosynthesis inhibitor **arylpyridazinone** prepn; **arylpyridazinone** prepn prostaglandin endoperoxide H synthase biosynthesis inhibitor; cyclooxygenase 2 selective inhibitor **arylpyridazinone** prepn; analgesic **arylpyridazinone** prepn; antipyretic **arylpyridazinone** prepn; antiinflammatory **arylpyridazinone** prepn; rheumatoid arthritis **arylpyridazinone** prepn; osteoarthritis **arylpyridazinone** prepn; antiarthritic **arylpyridazinone** prepn; antitumor **arylpyridazinone** prepn

IT Analgesics
Anti-inflammatory agents
Antiarthritics
Antipyretics
Antitumor agents
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT Osteoarthritis
(treatment of; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 655-20-9P 2514-18-3P 14092-00-3P 28075-50-5P 34837-84-8P
40400-25-7P 51437-00-4P, 1-Bromo-4-fluoro-3-methylbenzene 59982-04-6P
63031-77-6P 84956-71-8P 89981-03-3P 97137-16-1P 98546-51-1P
109715-47-1P 134965-39-2P 161886-22-2P, 3,4-Difluorophenylhydrazine
213764-19-3P 221025-49-6P 221025-50-9P 221025-51-0P 221030-72-4P
221030-73-5P 221030-74-6P 221030-75-7P 221030-76-8P 221030-77-9P
221030-78-0P 221030-79-1P 221030-80-4P 221030-81-5P 221030-82-6P
221030-83-7P 221030-84-8P 221030-85-9P 221030-86-0P 221030-87-1P
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221031-38-5P 221031-39-6P 221031-40-9P 221031-41-0P 266320-87-0P
266320-88-1P 266320-89-2P 266320-90-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 39391-18-9, Prostaglandin endoperoxide H synthase
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 109715-46-0 266320-84-7 266320-85-8 266320-86-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 221031-64-7P 221031-65-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 62-53-3, Benzenamine, reactions 65-85-0, Benzoic acid, reactions 67-63-0, 2-Propanol, reactions 70-11-1, 2-Bromoacetophenone 71-36-3, n-Butanol, reactions 75-31-0, 2-Aminopropane, reactions 75-33-2, Isopropyl mercaptan 75-65-0, Tert-Butanol, reactions 75-66-1, 2-Methyl-2-propanethiol 75-84-3 78-83-1, Reactions, reactions 87-56-9, Mucochloric acid 92-66-0, 4-Bromobiphenyl 92-69-3, 4-Phenylphenol 96-41-3, Cyclopentanol 97-95-0, 2-Ethyl-1-butanol 98-00-0, 2-(Hydroxymethyl)furan 98-02-2, Furfuryl mercaptan 98-59-9, p-Toluenesulfonyl chloride 99-07-0, 3-(Dimethylamino)phenol 100-11-8 100-39-0 100-44-7, reactions 100-51-6, Benzyl alcohol, reactions 100-53-8, Benzyl mercaptan 101-55-3, 4-Bromodiphenylether 102-56-7, 2,5-Dimethoxyaniline 103-63-9, (2-Bromoethyl)benzene 103-67-3, N-Methylbenzylamine 103-90-2 104-76-7 104-95-0, 4-Bromothioanisole 106-37-6, 1,4-Dibromobenzene 106-38-7, 1-Bromo-4-methylbenzene 106-39-8, 4-Bromo-1-chlorobenzene 106-41-2, p-Bromophenol 106-48-9, p-Chlorophenol 106-96-7, Propargyl bromide 107-18-6, 2-Propen-1-ol, reactions 107-82-4, 1-Bromo-3-methylbutane 108-01-0 108-11-2, 4-Methyl-2-pentanol 108-36-1, 1,3-Dibromobenzene 108-37-2, 1-Bromo-3-chlorobenzene 108-85-0, Cyclohexyl bromide 108-91-8, Cyclohexanamine, reactions 108-93-0, Cyclohexanol, reactions 108-94-1, Cyclohexanone, reactions 108-95-2, Phenol, reactions 109-00-2, 3-Hydroxypyridine 109-59-1, 2-(Isopropoxy)ethanol 110-63-4, 1,4-Butanediol, reactions 110-87-2 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 116-09-6, Acetol 120-20-7, 3,4-Dimethoxyphenethylamine 123-51-3 123-75-1, Pyrrolidine, reactions 126-30-7 137-43-9, Cyclopentyl bromide 150-76-5, 4-Methoxyphenol 151-18-8 156-87-6, 3-Hydroxypropylamine 339-62-8 348-57-2, 2,4-Difluorobromobenzene 348-61-8, 1-Bromo-3,4-difluorobenzene 349-55-3, 3-Methoxy-5-(trifluoromethyl)aniline 352-13-6, 4-Fluorophenylmagnesium bromide 352-34-1, 4-Fluoroiodobenzene 353-83-3, 2-Iodo-1,1,1-trifluoroethane 363-80-4, 2,3,5-Trifluoroaniline 367-11-3, 1,2-Difluorobenzene 367-25-9, 2,4-Difluoroaniline 367-67-9, 2-Bromo-5-nitrobenzotrifluoride 368-78-5, 3-(Trifluoromethyl)phenylhydrazine 371-14-2 371-40-4, 4-Fluoroaniline 371-41-5, 4-Fluorophenol 372-19-0, 3-Fluoroaniline 372-20-3, 3-Fluorophenol 383-53-9, 2-Bromo-4'-(trifluoromethyl)acetophenone 395-44-8, 2-(Trifluoromethyl)benzyl bromide 401-81-0 402-43-7, 1-Bromo-4-trifluoromethylbenzene 403-41-8, 4-Fluoro-α-methylbenzyl alcohol 405-50-5, 4-Fluorophenylacetic acid 456-41-7, 3-Fluorobenzyl bromide 459-46-1, 4-Fluorobenzyl bromide 460-25-3, 1,3-Dibromo-1,1-difluoropropane 461-96-1, 3,5-Difluorobromobenzene 488-11-9, Mucobromic acid 513-44-0, 2-Methyl-1-propanethiol 536-38-9, 2-Bromo-4'-chloroacetophenone 541-73-1 556-96-7, 5-Bromo-m-xylene

558-43-0, 2-Methyl-1,2-propanediol 563-47-3, 3-Chloro-2-methylpropene 577-19-5, 1-Bromo-2-nitrobenzene 589-35-5 590-90-9, 4-Hydroxy-2-butanone 591-17-3, 3-Bromotoluene 600-36-2, 2,4-Dimethyl-3-pentanol 619-57-8, 4-Hydroxybenzamide 622-26-4, 4-(2-Hydroxyethyl)piperidine 622-40-2, 4-(2-Hydroxyethyl)morpholine 623-00-7, 4-Bromobenzonitrile 624-95-3, 3,3-Dimethyl-1-butanol 626-88-0, 1-Bromo-4-methylpentane 626-89-1, 4-Methyl-1-pentanol 627-59-8, 5-Methyl-2-hexanol 636-98-6, 1-Iodo-4-nitrobenzene 645-56-7, 4-(n-Propyl)phenol 661-69-8, Hexamethylditin 700-57-2, 2-Adamantanol 701-34-8, 4-Aminosulfonyl-1-bromobenzene 763-32-6 763-89-3 765-58-2, 2-Bromo-5-**methylthiophene** 766-00-7, Cyclopentaneethanol 766-02-9, 2-Cyclopentene-1-ethanol 767-00-0, 4-Cyanophenol 823-85-8, 4-Fluorophenylhydrazine hydrochloride 870-63-3 873-74-5, 4-Aminobenzonitrile 924-41-4, 1,5-Hexadien-3-ol 931-51-1, Cyclohexylmagnesium chloride 1003-03-8, Cyclopentylamine 1003-09-4, 2-**Bromothiophene** 1072-85-1, 2-Fluorobromobenzene 1073-62-7, Benzylhydrazine hydrochloride 1121-86-4, 1-Fluoro-3-iodobenzene 1126-81-4, 4-**Acetamidothiophenol** 1423-26-3 1462-03-9, 1-Methyl-1-cyclopentanol 1521-51-3, 3-Bromocyclohexene 1544-53-2 1569-69-3, Cyclohexyl mercaptan 1643-73-8, 4-Fluorobenzylmagnesium chloride 1679-07-8, Cyclopentyl mercaptan 1679-18-1, 4-Chlorobenzeneboronic acid 1698-53-9, 2-Phenyl-4,5-dichloro-3(2H)-**pyridazinone** 1765-40-8, 2,3,4,5,6-Pentafluorobenzyl bromide 1765-93-1, 4-Fluorobenzeneboronic acid 1794-48-5 1826-67-1, Vinylmagnesium bromide 1996-29-8, 1-Bromo-4-chloro-2-fluorobenzene 2039-86-3, 3-Bromostyrene 2076-88-2, 2-(Chloromethyl)benzo[b] **thiophene** 2081-44-9, 4-Tetrahydropyranol 2113-57-7, 3-Bromobiphenyl 2156-04-9 2259-30-5, Tert-Butylmagnesium bromide 2312-23-4, 3-Chlorophenylhydrazine hydrochloride 2357-52-0, 3-Fluoro-4-methoxybromobenzene 2417-72-3, Methyl 4-(bromomethyl)benzoate 2516-33-8, Cyclopropylmethanol 2516-34-9, Cyclobutanamine 2516-47-4, Cyclopropanemethanamine 2517-43-3 2557-78-0, 2-**Fluorothiophenol** 2566-44-1, 2-(Cyclopropyl)ethanol 2567-14-8, 1,1,3-Trichloropropene 2568-33-4 2637-34-5, 2-Mercaptopyridine 2746-14-7, 1-Methylcyclopropanemethanol 2746-23-8, 3-(Chloromethyl) **thiophene** 2799-16-8 2873-18-9, 2-Bromo-5-**chlorothiophene** 2924-16-5, 3-Fluorophenylhydrazine hydrochloride 2938-98-9, 2-Methyl-1,4-butanediol 3179-31-5, 1H-1,2,4-Triazole-3-thiol 3446-89-7, 4-Methylthiobenzaldehyde 3863-11-4 3958-57-4, 3-Nitrobenzyl bromide 3972-65-4, 1-Bromo-4-tert-butylbenzene 4254-29-9, 2-Indanol 4294-57-9, p-Tolylmagnesium bromide 4377-41-7, 2-(Chloromethyl)quinoline 4392-24-9, Cinnamyl bromide 4399-47-7, Cyclobutyl bromide 4548-78-1, 3-Methylbutylmagnesium bromide 4795-29-3, Tetrahydrofurfurylamine 5036-48-6, 1H-Imidazole-1-propanamine 5042-30-8, Trifluoroethylhydrazine 5271-38-5, 2-(Methylthio)ethanol 5332-73-0, 3-Methoxypropylamine 5362-55-0 5469-26-1, 1-Bromopinacolone 5673-98-3 5674-02-2, Isobutylmagnesium chloride 5713-61-1, 2-Thienylmagnesium bromide 5720-05-8, 4-Methylphenylboronic acid 5720-06-9, 2-Methoxybenzeneboronic acid 5788-58-9, 4,5-Dibromo-3(2H)-**pyridazinone** 6165-69-1, **Thiophene**-3-boronic acid 6351-10-6, 1-Indanol 6630-33-7, 2-Bromobenzaldehyde 6738-06-3, Phenylacetylenemagnesium bromide 6921-34-2, Benzylmagnesium chloride 7051-34-5 7342-82-7, 3-**Bromobenzothiophene** 7400-27-3, Tert-Butylhydrazine hydrochloride 7417-21-2, 2-(3,4-Dimethoxyphenyl)ethanol 7429-94-9 10493-44-4 13124-18-0, 3,4-Dichlorophenylhydrazine 13195-50-1, 2-Bromo-5-**nitrothiophene** 13291-18-4, Isopropenylmagnesium bromide 13331-27-6, 3-Nitrobenzeneboronic acid 14114-05-7, Cyclopropyltriphenylphosphonium bromide 14282-76-9, 2-Bromo-3-**methylthiophene** 14300-71-1 14763-20-3 14763-60-1, 4-(Methylsulfonyl)phenol 14916-80-4, 3-Octyn-1-ol 15894-04-9

16419-60-6 16466-97-0 18729-48-1, 3-Methylcyclopentanol 19477-73-7, 6-Bromophthalide 19614-16-5, 2-Bromothioanisole 20099-89-2, 2-Bromo-4'-cyanoacetophenone 22037-28-1, 3-Bromofuran 22884-29-3, Isobutyltriphenylphosphonium bromide 23915-07-3, 2,4-Difluorobenzyl bromide 24070-77-7, 2-Methylcyclopentanol 26167-44-2, 3-Chloroacetylbenzo[b]**thiophene** 26445-03-4, Thiocresol 27246-81-7, 3-Bromophenylhydrazine hydrochloride 27314-17-6 28322-40-9, Isoamyltriphenylphosphonium bromide 32916-51-1, Cyclopentylmagnesium chloride 33577-16-1, Methyl(methylsulfinylmethyl)sulfide 33598-19-5 33733-73-2, 3-Bromothioanisole 33884-43-4, 2-(2-Bromoethyl)-1,3-dioxane 34698-41-4, 1-Indanylamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 35166-78-0, Cyclohexylmethylmagnesium bromide 37677-17-1, 1-Bromomethylcyclohexene 39720-27-9, 4-(Chloromethyl)phenyl acetate 40594-37-4, 3,4-Difluorophenylhydrazine hydrochloride 40811-49-2, 2-(Isopropylthio)ethanol 50398-79-3, 2-(Bromomethyl)-5-**chlorothiazole** 51336-94-8, 2-Chloro-2',4'-difluoroacetophenone 51755-66-9, 3-(Methylthio)-1-hexanol 52497-07-1, 1,3-Dichloro-1-butene 54751-01-8, 4-(Bromomethyl)pyridine 55401-97-3, 2-(Bromomethyl)pyridine 55499-43-9 55766-17-1 56816-01-4, Ethyl (S)-3-hydroxybutanoate 58114-09-3 59311-22-7 59311-24-9 60811-18-9, 4-Bromo-1-chloro-2-fluorobenzene 60811-21-4 60811-23-6, 3-Chloro-4-**fluorothiophenol** 62087-82-5, 1-Adamantyl fluoroformate 64168-34-9, 3-Fluorobenzylmagnesium chloride 65130-46-3 69966-55-8, 3-(Bromomethyl)pyridine 72396-61-3 72657-23-9 80657-57-4, Methyl (S)-3-hydroxy-2-methylpropionate 82297-89-0, 4-Fluoro-3-methylphenylmagnesium bromide 84282-78-0 85118-01-0, 3,4-Difluorobenzyl bromide 85676-85-3 90555-66-1 90878-19-6, Phenethylmagnesium chloride 92636-36-7 93777-26-5, 5-Bromo-2-fluorobenzaldehyde 98437-24-2, 2-Benzofuranboronic acid 103962-10-3, 2-Bromo-4'-(trifluoromethoxy)acetophenone 112615-82-4, 5-Methylhexylmagnesium bromide 122957-82-8 124050-15-3, 2-(Chloromethyl)-6-fluoroquinoline 128758-41-8 128796-39-4, 4-(Trifluoromethyl)benzeneboronic acid 134150-01-9 137504-86-0, 3-Fluoro-4-chlorophenylboronic acid 141483-15-0, 2-Fluoro-5-trifluoromethylphenol 144432-85-9, 3-Chloro-4-fluorobenzeneboronic acid 149507-26-6 151411-98-2 157911-55-2 157911-56-3 162125-08-8, 3,4-Dichlorophenylboronic acid 162607-18-3 163105-90-6 168267-99-0 171497-20-4 172975-69-8 175135-73-6 175135-74-7 208641-98-9 221020-96-8 221031-42-1 221031-43-2 221031-44-3 221031-45-4 221031-46-5 221031-47-6 221031-48-7 221031-49-8 221031-50-1 221031-51-2 221031-52-3 221031-53-4 221031-54-5 221031-55-6 221031-56-7 221031-57-8 221031-58-9 221031-59-0 221031-60-3 221031-61-4 221031-62-5 221031-63-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 213763-90-7P 213764-00-2P 213764-17-1P 221025-44-1P 221025-45-2P 221025-46-3P 221025-47-4P 221025-52-1P 221025-53-2P 221025-77-0P 221026-16-0P 221026-30-8P 221026-34-2P 221026-35-3P 221026-45-5P 221026-46-6P 221026-51-3P 221026-61-5P 221026-62-6P 221026-78-4P 221027-19-6P 221027-24-3P 221027-36-7P 221027-91-4P 221027-98-1P 221028-16-6P 221028-18-8P 221028-23-5P 221028-31-5P 221028-43-9P 221028-45-1P 221029-22-7P 221029-24-9P 221029-25-0P 221029-26-1P 221029-28-3P 221029-32-9P 221029-41-0P 221029-43-2P 221029-46-5P 221029-47-6P 221029-50-1P 221029-69-2P 221029-78-3P 221029-80-7P 221029-81-8P 221029-83-0P 221029-84-1P 221029-86-3P 221030-47-3P 221030-56-4P 221030-64-4P 221030-66-6P 221030-67-7P 266320-83-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 213763-92-9P 213763-94-1P 213763-98-5P 213763-99-6P 213764-11-5P
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221025-73-6P **221025-74-7P** 221025-75-8P 221025-76-9P
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221025-92-9P 221025-94-1P 221025-96-3P **221025-98-5P**
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 221028-67-7P 221028-68-8P 221028-69-9P 221028-70-2P 221028-71-3P
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266319-76-0P 266319-77-1P 266319-78-2P 266319-79-3P 266319-80-6P
266319-81-7P 266319-82-8P 266319-83-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 266319-84-0P 266319-85-1P 266319-86-2P 266319-87-3P 266319-88-4P
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266319-99-7P 266320-00-7P 266320-01-8P 266320-02-9P 266320-03-0P
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 39391-18-9

RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(target compound; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

RETABLE

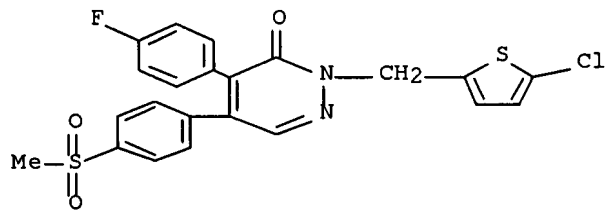
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Abbott Laboratories Usa	1999			WO 9910331 A	HCAPLUS
Abbott Laboratories Usa	1999			WO 9910332 A	HCAPLUS
Merck Frosst Canada Inc	1998			WO 9841511 A	HCAPLUS

IT **221025-73-6P 221025-74-7P 221025-98-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

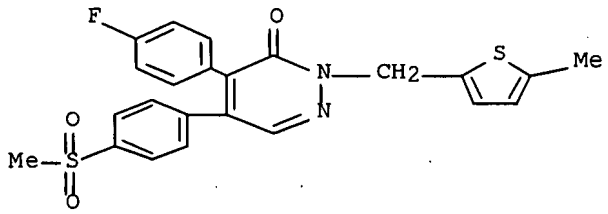
RN 221025-73-6 HCAPLUS

CN 3(2H)-Pyridazinone, 2-[(5-chloro-2-thienyl)methyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

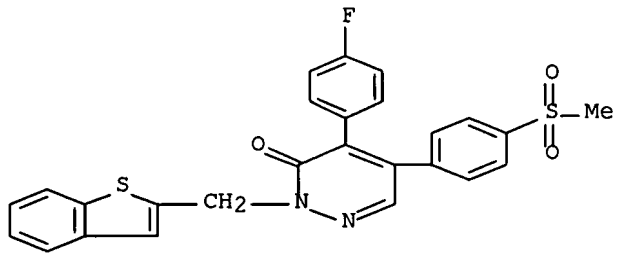


RN 221025-74-7 HCAPLUS

CN 3(2H)-Pyridazinone, 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-2-[(5-methyl-2-thienyl)methyl]- (9CI) (CA INDEX NAME)



RN 221025-98-5 HCAPLUS
CN 3(2H)-Pyridazinone, 2-(benzo[b]thien-2-ylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



L99 ANSWER 9 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 9
ACCESSION NUMBER: 2000:161290 HCAPLUS Full-text
DOCUMENT NUMBER: 132:194389
TITLE: Preparation of thieno[2,3-d]pyrimidine-2,4(1H,3H)-diones as immunosuppressants
INVENTOR(S): Bantick, John; Cooper, Martin; Perry, Matthew; Thorne, Philip
PATENT ASSIGNEE(S): Astra Pharmaceuticals Ltd., UK; Astra Aktiebolag
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012514	A1	20000309	WO 1999-SE1400	19990818 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2339664	A1	20000309	CA 1999-2339664	19990818 <--
AU 9957677	A1	20000321	AU 1999-57677	19990818 <--
AU 763758	B2	20030731		

EP 1107973	A1	20010620	EP 1999-944964	19990818 <--
EP 1107973	B1	20031105		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002523511	T	20020730	JP 2000-567536	19990818 <--
NZ 509809	A	20021126	NZ 1999-509809	19990818 <--
AT 253580	T	20031115	AT 1999-944964	19990818 <--
PT 1107973	T	20040331	PT 1999-944964	19990818 <--
ES 2211161	T3	20040701	ES 1999-944964	19990818 <--
US 6300334	B1	20011009	US 1999-402837	19991013 <--
PRIORITY APPLN. INFO.:			SE 1998-2895 A	19980828 <--
			WO 1999-SE1400 W	19990818 <--

OTHER SOURCE(S): MARPAT 132:194389

ED Entered STN: 10 Mar 2000

AB The title compds. (I) [wherein R = C(O)Ar1 or C(R4)(R5)Ar1;R1 and R2 = independently H, (cyclo)alkyl, alkenyl, or cycloalkylmethyl; R3 = H or XR9 or XAr2; R4 = H or alkyl; R5 = H or OH; R9 = Me optionally substituted by 1 or more CN, CO2H, alkoxycarbonyl, tetrazolyl, (un)substituted carboxyamido; R10 = H, alkyl, or R9; X = O, S(O)n, C(O)NR10, C(O)O, NHC(O)NR10, NHC(O)O, or SO2NR10; Ar1 = (un)substituted heteroaryl, Ar2 = (un)substituted Ph, pyridinyl, thienyl, pyridone, or pyridine N-oxide; n = 0-2] were prepared as immunosuppressants. for the treatment of reversible obstructive airway diseases, such as asthma, bronchitis, and rhinitis. For example, II was formed in a 4-step sequence involving (1) N-addition of 1-iodo-2-methylpropane to 6-chloro-3-methyl-1H-pyrimidine-2,4-(1H,3H)- dione, (2) thiolation of the chloro compound with NaSH.H2O, (3) cycloaddn. of the 6-thioxopyrimidinedione with aqueous ClCH2CHO, and (4) coupling of the thienopyrimidinedione with 1-methylbenzimidazole-2-carboxaldehyde. In a PMA/ionomycin-stimulated peripheral blood mononuclear cell (PBMC) proliferation assay, I exhibited IA50 values of < 1 μM.

IC ICM C07D495-04
ICS A61K031-505

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 51-17-2, Benzimidazole 75-33-2, 1-Methylethanethiol 77-76-9, 2,2-Dimethoxypropane 81-07-2, Saccharin 85-41-6, Isoindole-1,3-dione 95-14-7, 1H-Benzotriazole 95-16-9, **Benzothiazole** 98-03-3, 2-**Thiophenecarboxaldehyde** 105-56-6, Ethyl cyanoacetate 123-75-1, Pyrrolidine, reactions 271-44-3, 1H-Indazole 271-63-6, 1H-Pyrrolo[2,3-b]pyridine 498-62-4, 3-**Thiophenecarboxaldehyde** 500-22-1, 3-Pyridinecarboxaldehyde 513-38-2, 1-Iodo-2-methylpropane 617-35-6, Ethyl pyruvate 872-85-5, 4-Pyridinecarboxaldehyde 1121-60-4, 2-Pyridinecarboxaldehyde 1445-69-8, Phthalhydrazide 1759-53-1, Cyclopropanecarboxylic acid 2799-21-5, (R)-3-Hydroxypyrrolidine 3012-80-4, 1-Methylbenzimidazole-2-carboxaldehyde 4318-56-3 4857-06-1, 2-Chloro-1H-benzimidazole 7051-34-5, Cyclopropylmethyl bromide 7283-96-7, 5-Chloro-2-**thiophenecarboxaldehyde** 7774-74-5, 2-**Mercaptothiophene** 10200-59-6, 2-**Thiazolecarboxaldehyde** 19721-22-3, 3-Mercaptopropanol 31891-06-2, 2-Amino-3-**ethoxycarbonylthiophene** 33821-94-2, 1-Bromo-3-(2-tetrahydropyranyl)oxypropane 36520-39-5, Azetidine hydrochloride 75860-86-5 175204-81-6, 4-Chloro-1-methyl-1H-pyrazole-3-carboxaldehyde 189278-27-1, 2-Bromo-6-trifluoromethylpyridine
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of thieno[2,3-d]pyrimidine-2,4(1H,3H)-diones as immunosuppressants)

IT 259861-27-3P 259861-28-4P 259861-29-5P 259861-30-8P 259861-31-9P
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259861-56-8P 259861-59-1P 259861-63-7P 259861-65-9P 259861-66-0P
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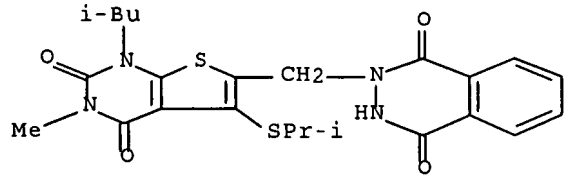
259861-93-3P 259861-94-4P 259861-95-5P 259861-96-6P 259861-97-7P
259861-98-8P **259861-99-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of thieno[2,3-d]pyrimidine-2,4(1H,3H)-diones as
immunosuppressants)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Arzneimittelwerk Dresde	1991			DD 293824 A5	HCAPLUS
Fukumi, H	1989			JP 1213284 A	
Gutschow, M	1995	328	231	Arch Pharm (Weinheim	MEDLINE
Takeda Chemical Industr	1995			EP 0640606 A1	HCAPLUS

IT **259861-99-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of thieno[2,3-d]pyrimidine-2,4(1H,3H)-diones as
immunosuppressants)
RN 259861-99-9 HCAPLUS
CN 1,4-Phthalazinedione, 2,3-dihydro-2-[[1,2,3,4-tetrahydro-3-methyl-5-[(1-methylethyl)thio]-1-(2-methylpropyl)-2,4-dioxothieno[2,3-d]pyrimidin-6-yl]methyl]- (9CI) (CA INDEX NAME)



L99 ANSWER 10 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 10
ACCESSION NUMBER: 1999:166604 HCAPLUS Full-text
DOCUMENT NUMBER: 130:223284
TITLE: Preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors
INVENTOR(S): Black, Lawrence A.; Basha, Anwer; Kolasa, Teodozyj; Kort, Michael E.; Liu, Huaqing; McCarty, Catherine M.; Patel, Meena V.; Rohde, Jeffrey J.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 307 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9910331	A1	19990304	WO 1998-US16479	19980810 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2299300	A1	19990304	CA 1998-2299300	19980810 <--
AU 9886976	A	19990316	AU 1998-86976	19980810 <--
AU 741317	B2	20011129		
EP 1007515	A1	20000614	EP 1998-938451	19980810 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
BR 9812127	A	20000718	BR 1998-12127	19980810 <--
TR 200000478	T2	20020422	TR 2000-200000478	19980810 <--
JP 2003516925	T	20030520	JP 2000-507660	19980810 <--
HU 200400909	A2	20040728	HU 2004-909	19980810 <--
IL 133552	A	20051218	IL 1998-133552	19980810 <--
ZA 9807555	A	19990223	ZA 1998-7555	19980820 <--
TW 232216	B	20050511	TW 1998-87113837	19980910 <--
NO 2000000863	A	20000222	NO 2000-863	20000222 <--
NO 315423	B1	20030901		
MX 200001850	A	20001030	MX 2000-1850	20000222 <--
BG 104241	A	20001031	BG 2000-104241	20000315 <--
BG 64675	B1	20051130		
PRIORITY APPLN. INFO.:			US 1997-917023 A	19970822 <--
			US 1998-129570 A	19980805 <--
			WO 1998-US16479 W	19980810 <--

OTHER SOURCE(S): MARPAT 130:223284

ED Entered STN: 15 Mar 1999

AB The title compds. [I; X = O, S, NR4, etc.; R4 = alkyl, alkenyl, cycloalkyl, etc.; R = H, alkyl, alkenyl, etc.; at least one of R1-R3 = II-III (wherein X1 = SO2, SO(NR10), SO, etc.; R9 = alkyl, alkenyl, alkynyl, etc.; X2 = H, halo, alkyl, etc.; R10 = H, alkyl, cycloalkyl); the remaining two of the groups of R1-R3 = H, OH, hydroxyalkyl, etc.] which are cyclooxygenase (COX) inhibitors, and in particular, are selective inhibitors of cyclooxygenase-2 (COX-2), and therefore are useful in treating pain, fever, inflammation, rheumatoid arthritis, osteoarthritis, adhesions, and cancer, were prepared Thus, oxidation of 2-benzyl-4-(4- fluorophenyl)-5-[4-(methylthio)phenyl]-3(2H)-**pyridazinone** (preparation given) with MeCO3H in CH2Cl2 afforded 86% I [X = O; R = PhCH2; R1 = 4-FC6H4; R2 = 4-(MeSO2)C6H4; R3 = H] which showed 0.014 μM against COX-2. COX-2 is the inducible isoform associated with inflammation, as opposed to the constitutive isoform, cyclooxygenase-1 (COX-1) which is an important "housekeeping" enzyme in many tissues, including the gastrointestinal (GI) tract and the kidneys. The selectivity of the compds. I for COX-2 minimizes the unwanted GI and renal side-effects seen with currently marketed non-steroidal anti-inflammatory drugs (NSAIDs).

IC ICM C07D237-14
ICS C07D401-06; C07D403-06; C07D237-18; C07D409-06; C07D413-06; C07D405-06; A61K031-50; C07F011-00

CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST prostaglandin endoperoxide H synthase biosynthesis inhibitor **arylpyridazinone** prepn; **arylpyridazinone** prepn prostaglandin endoperoxide H synthase biosynthesis inhibitor;

cyclooxygenase 2 selective inhibitor **arylpyridazinone** prepn; analgesic **arylpyridazinone** prepn; antipyretic **arylpyridazinone** prepn; antiinflammatory **arylpyridazinone** prepn; rheumatoid arthritis **arylpyridazinone** prepn; osteoarthritis **arylpyridazinone** prepn; antiarthritic **arylpyridazinone** prepn; antitumor **arylpyridazinone** prepn

IT Analgesics
Anti-inflammatory agents
Antiarthritics
Antipyretics
Antitumor agents
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT Osteoarthritis
(treatment of; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 39391-18-9
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(2; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 213763-90-7P 213764-00-2P 213764-17-1P 221025-44-1P 221025-45-2P
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221030-64-4P 221030-66-6P 221030-67-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 213763-92-9P 213763-94-1P 213763-98-5P 213763-99-6P 213764-11-5P
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221028-62-2P 221028-63-3P 221028-64-4P 221028-65-5P 221028-66-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 221028-67-7P 221028-68-8P 221028-69-9P 221028-70-2P 221028-71-3P
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221030-71-3P 221035-92-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 39391-18-9, Prostaglandin endoperoxide H synthase
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 62-53-3, Aniline, reactions 65-85-0, Benzoic acid, reactions 67-63-0, 2-Propanol, reactions 70-11-1, 2-Bromoacetophenone 75-31-0, 2-Aminopropane, reactions 75-33-2, Isopropyl mercaptan 75-65-0, tert-Butanol, reactions 75-66-1, 2-Methyl-2-propanethiol 75-84-3 78-83-1, reactions 87-56-9, Mucochloric acid 92-66-0, 4-Bromobiphenyl 92-69-3, 4-Phenylphenol 96-41-3, Cyclopentanol 97-95-0, 2-Ethyl-1-butanol 98-00-0, 2-(Hydroxymethyl)furan 98-02-2, Furfuryl mercaptan 98-59-9, p-Toluenesulfonyl chloride 99-07-0, 3-(Dimethylamino)phenol 100-11-8 100-39-0, Benzyl bromide 100-44-7, reactions 100-51-6, Benzyl alcohol, reactions 100-53-8, Benzyl mercaptan 101-55-3, 4-Bromodiphenylether 102-56-7, 2,5-Dimethoxyaniline 103-63-9, (2-Bromoethyl)benzene 103-67-3, N-Methylbenzylamine 103-90-2, 4-Acetamidophenol 104-76-7 104-95-0, 4-Bromothioanisole 106-37-6, 1,4-Dibromobenzene 106-38-7, 1-Bromo-4-methylbenzene 106-39-8, 4-Bromo-1-chlorobenzene 106-41-2, p-Bromophenol 106-48-9, p-Chlorophenol 106-96-7, Propargyl bromide 107-18-6, 2-Propen-1-ol, reactions 107-82-4, 1-Bromo-3-methylbutane 108-01-0, N,N-(Dimethyl)ethanolamine 108-11-2, 4-Methyl-2-pentanol 108-36-1, 1,3-Dibromobenzene 108-37-2, 1-Bromo-3-chlorobenzene 108-85-0, Cyclohexyl bromide 108-91-8, Cyclohexylamine, reactions 108-93-0, Cyclohexanol, reactions 108-94-1, Cyclohexanone, reactions 108-95-2, Phenol, reactions 109-00-2, 3-Hydroxypyridine 109-59-1, 2-(Isopropoxy)ethanol 110-87-2 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 116-09-6, Acetol 120-20-7, 3,4-Dimethoxyphenethylamine 123-51-3, 3-Methyl-1-butanol 123-75-1, Pyrrolidine, reactions 137-43-9, Cyclopentyl bromide 150-76-5, 4-Methoxyphenol 151-18-8 156-87-6, 3-Hydroxypropylamine 339-62-8 348-57-2, 2,4-Difluorobromobenzene 348-61-8, 1-Bromo-3,4-difluorobenzene 349-55-3, 3-Methoxy-5-(trifluoromethyl)aniline 352-13-6, 4-Fluorophenylmagnesium bromide 352-34-1, 4-Fluoroiodobenzene 353-83-3, 2-Iodo-1,1,1-trifluoroethane 363-80-4, 2,3,5-Trifluoroaniline 367-11-3, 1,2-Difluorobenzene 367-25-9, 2,4-Difluoroaniline 367-67-9, 2-Bromo-5-nitrobenzotrifluoride 371-40-4, 4-Fluoroaniline 371-41-5, 4-Fluorophenol 372-19-0, 3-Fluoroaniline 372-20-3, 3-Fluorophenol 383-53-9, 2-Bromo-4'-(trifluoromethyl)acetophenone 395-44-8, 2-(Trifluoromethyl)benzyl bromide 401-81-0 402-43-7, 1-Bromo-4-trifluoromethylbenzene 403-41-8, 4-Fluoro-α-methylbenzyl alcohol 405-50-5, 4-Fluorophenylacetic acid 456-41-7, 3-Fluorobenzyl bromide 459-46-1, 4-Fluorobenzyl bromide 460-25-3, 1,3-Dibromo-1,1-difluoropropane 461-96-1, 3,5-Difluorobromobenzene 488-11-9, Mucobromic acid 513-44-0, 2-Methyl-1-propanethiol 536-38-9, 2-Bromo-4'-chloroacetophenone 541-73-1 556-96-7, 5-Bromo-m-xylene 558-43-0, 2-Methyl-1,2-propanediol 563-47-3, 3-Chloro-2-methylpropene 577-19-5, 1-Bromo-2-nitrobenzene 589-35-5 590-90-9, 4-Hydroxy-2-butanone 591-17-3, 3-Bromotoluene 600-36-2, 2,4-Dimethyl-3-pentanol 619-57-8, 4-Hydroxybenzamide 622-26-4,

4-(2-Hydroxyethyl)piperidine 622-40-2, 4-(2-Hydroxyethyl)morpholine 623-00-7, 4-Bromobenzonitrile 624-95-3, 3,3-Dimethyl-1-butanol 626-88-0, 1-Bromo-4-methylpentane 626-89-1, 4-Methyl-1-pentanol 627-59-8, 5-Methyl-2-hexanol 636-98-6, 1-Iodo-4-nitrobenzene 645-56-7, 4-(n-Propyl)phenol 661-69-8, Hexamethylditin 700-57-2, 2-Adamantanol 701-34-8, 4-Aminosulfonyl-1-bromobenzene 763-32-6 763-89-3 765-58-2, 2-Bromo-5-**methylthiophene** 766-00-7, Cyclopentaneethanol 766-02-9, 2-Cyclopentene-1-ethanol 767-00-0, 4-Cyanophenol 823-85-8, 4-Fluorophenylhydrazine hydrochloride 870-63-3 873-74-5, 4-Aminobenzonitrile 924-41-4, 1,5-Hexadien-3-ol 931-51-1, Cyclohexylmagnesium chloride 1003-03-8, Cyclopentylamine 1003-09-4, 2-**Bromothiophene** 1072-85-1, 2-Fluorobromobenzene 1073-62-7, Benzylhydrazine hydrochloride 1121-86-4, 1-Fluoro-3-iodobenzene 1126-81-4, 4-**Acetamidothiophenol** 1423-26-3 1462-03-9, 1-Methyl-1-cyclopentanol 1521-51-3, 3-Bromocyclohexene 1544-53-2 1569-69-3, Cyclohexyl mercaptan 1643-73-8, 4-Fluorobenzylmagnesium chloride 1679-07-8, Cyclopentyl mercaptan 1679-18-1, 4-Chlorobenzeneboronic acid 1698-53-9, 2-Phenyl-4,5-dichloro-3(2H)-**pyridazinone** 1765-40-8, 2,3,4,5,6-Pentafluorobenzyl bromide 1765-93-1, 4-Fluorobenzeneboronic acid 1794-48-5 1826-67-1, Vinylmagnesium bromide 1996-29-8, 1-Bromo-4-chloro-2-fluorobenzene 2039-86-3, 3-Bromostyrene 2076-88-2, 2-(Chloromethyl)benzo[b] **thiophene** 2081-44-9, 4-Tetrahydropyranol 2113-57-7, 3-Bromobiphenyl 2156-04-9 2259-30-5, tert-Butylmagnesium bromide 2312-23-4, 3-Chlorophenylhydrazine hydrochloride 2357-52-0, 3-Fluoro-4-methoxybromobenzene 2417-72-3, Methyl 4-(bromomethyl)benzoate 2516-33-8, Cyclopropylmethanol 2516-34-9, Cyclobutylamine 2516-47-4, Cyclopropylmethylamine 2517-43-3 2557-78-0, 2-**Fluorothiophenol** 2566-44-1, 2-(Cyclopropyl)ethanol 2567-14-8, 1,1,3-Trichloropropene 2568-33-4 2637-34-5, 2-Mercaptopyridine 2746-14-7, 1-Methylcyclopropanemethanol 2746-23-8, 3-(Chloromethyl) **thiophene** 2799-16-8 2873-18-9, 2-Bromo-5-**chlorothiophene** 2924-16-5, 3-Fluorophenylhydrazine hydrochloride 2938-98-9, 2-Methyl-1,4-butanediol 3179-31-5, 1H-1,2,4-Triazole-3-thiol 3446-89-7, 4-Methylthiobenzaldehyde 3958-57-4, 3-Nitrobenzyl bromide 3972-65-4, 1-Bromo-4-tert-butylbenzene 4254-29-9, 2-Indanol 4294-57-9, p-Tolylmagnesium bromide 4377-41-7, 2-(Chloromethyl)quinoline 4392-24-9, Cinnamyl bromide 4399-47-7, Cyclobutyl bromide 4548-78-1, 3-Methylbutylmagnesium bromide 4795-29-3, Tetrahydrofurfurylamine 5036-48-6, 1H-Imidazole-1-propanamine 5042-30-8, Trifluoroethylhydrazine 5271-38-5, 2-(Methylthio)ethanol 5332-73-0, 3-Methoxypropylamine 5362-55-0 5469-26-1, 1-Bromopinacolone 5673-98-3 5674-02-2, Isobutylmagnesium chloride 5713-61-1, 2-Thienylmagnesium bromide 5720-05-8, 4-Methylphenylboronic acid 5720-06-9, 2-Methoxybenzeneboronic acid 5788-58-9, 4,5-Dibromo-3(2H)-**pyridazinone** 6165-69-1, **Thiophene**-3-boronic acid 6351-10-6, 1-Indanol 6630-33-7, 2-Bromobenzaldehyde 6738-06-3, Phenylacetylenemagnesium bromide 6921-34-2, Benzylmagnesium chloride 7051-34-5 7342-82-7, 3-**Bromobenzothiophene** 7400-27-3, tert-Butylhydrazine hydrochloride 7417-21-2, 2-(3,4-Dimethoxyphenyl)ethanol 7429-94-9 10493-44-4 13195-50-1, 2-Bromo-5-**nitrothiophene** 13291-18-4, Isopropenylmagnesium bromide 13331-27-6, 3-Nitrobenzeneboronic acid 14114-05-7, Cyclopropyltriphenylphosphonium bromide 14282-76-9, 2-Bromo-3-**methylthiophene** 14300-71-1 14763-60-1, 4-(Methylsulfonyl)phenol 14916-80-4, 3-Octyn-1-ol 15894-04-9 16419-60-6 16466-97-0 18729-48-1, 3-Methylcyclopentanol 19477-73-7, 6-Bromophthalide 19614-16-5, 2-Bromothioanisole 20099-89-2, 2-Bromo-4'-cyanoacetophenone 22037-28-1, 3-Bromofuran 22884-29-3, Isobutyltriphenylphosphonium bromide 23915-07-3, 2,4-Difluorobenzyl bromide 24070-77-7, 2-Methylcyclopentanol 26167-44-2,

3-Chloroacetylbenzo[b]**thiophene** 26445-03-4, Thiocresol 27246-81-7, 3-Bromophenylhydrazine hydrochloride 28322-40-9, Isoamyltriphenylphosphonium bromide 32916-51-1, Cyclopentylmagnesium chloride 33577-16-1, Methyl(methylsulfinylmethyl)sulfide 33598-19-5 33733-73-2, 3-Bromothioanisole 33884-43-4, 2-(2-Bromoethyl)-1,3-dioxane 34698-41-4, 1-Indanylamine 35166-78-0, Cyclohexylmethylmagnesium bromide 37677-17-1, 1-Bromomethylcyclohexene 39720-27-9, 4-(Chloromethyl)phenyl acetate 40594-37-4, 3,4-Difluorophenylhydrazine hydrochloride 40811-49-2, 2-(Isopropylthio)ethanol 50398-79-3, 2-(Bromomethyl)-5-**chlorothiazole** 51336-94-8, 2-Chloro-2',4'-difluoroacetophenone 51755-66-9, 3-(Methylthio)-1-hexanol 52497-07-1, 1,3-Dichloro-1-butene
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 54751-01-8, 4-(Bromomethyl)pyridine 55401-97-3, 2-(Bromomethyl)pyridine 55499-43-9 55766-17-1 58114-09-3 59311-22-7 59311-24-9 60811-18-9, 4-Bromo-1-chloro-2-fluorobenzene 60811-21-4 60811-23-6, 3-Chloro-4-**fluorothiophenol** 62087-82-5, 1-Adamantyl fluoroformate 64168-34-9, 3-Fluorobenzylmagnesium chloride 65130-46-3 69966-55-8, 3-(Bromomethyl)pyridine 72657-23-9 80657-57-4, Methyl (S)-3-hydroxy-2-methylpropionate 82297-89-0, 4-Fluoro-3-methylphenylmagnesium bromide 85118-01-0, 3,4-Difluorobenzyl bromide 85676-85-3 90555-66-1 90878-19-6, Phenethylmagnesium chloride 92636-36-7 93777-26-5, 5-Bromo-2-fluorobenzaldehyde 98437-24-2, 2-Benzofuranboronic acid 103962-10-3, 2-Bromo-4'-(trifluoromethoxy)acetophenone 112615-82-4, 5-Methylhexylmagnesium bromide 122957-82-8 124050-15-3, 2-(Chloromethyl)-6-fluoroquinoline 128796-39-4, 4-(Trifluoromethyl)benzeneboronic acid 134150-01-9 137504-86-0, 3-Fluoro-4-chlorophenylboronic acid 141483-15-0, 2-Fluoro-5-trifluoromethylphenol 144432-85-9, 3-Chloro-4-fluorobenzeneboronic acid 149507-26-6 151411-98-2 157911-55-2 157911-56-3 162125-08-8, 3,4-Dichlorophenylboronic acid 162607-18-3 163105-90-6 168267-99-0 171497-20-4 172975-69-8 175135-73-6 175135-74-7 208641-98-9 221020-96-8 221031-42-1 221031-43-2 221031-44-3 221031-45-4 221031-46-5 221031-47-6 221031-48-7 221031-49-8 221031-50-1 221031-51-2 221031-52-3 221031-53-4 221031-54-5 221031-55-6 221031-56-7 221031-57-8 221031-58-9 221031-59-0 221031-60-3 221031-61-4 221031-62-5 221031-63-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 655-20-9P 2514-18-3P 14092-00-3P 28075-50-5P 34837-84-8P 40400-25-7P 51437-00-4P, 1-Bromo-4-fluoro-3-methylbenzene 59982-04-6P 63031-77-6P 84956-71-8P 89981-03-3P 97137-16-1P 98546-51-1P 134965-39-2P 213764-19-3P 221025-49-6P 221025-50-9P 221025-51-0P 221030-72-4P 221030-73-5P 221030-74-6P 221030-75-7P 221030-76-8P 221030-77-9P 221030-78-0P 221030-79-1P 221030-80-4P 221030-81-5P 221030-82-6P 221030-83-7P 221030-84-8P 221030-85-9P 221030-86-0P 221030-87-1P 221030-88-2P 221030-89-3P 221030-90-6P 221030-91-7P 221030-92-8P 221030-93-9P 221030-94-0P 221030-95-1P 221030-96-2P 221030-97-3P 221030-98-4P 221030-99-5P 221031-00-1P 221031-01-2P 221031-02-3P 221031-03-4P 221031-04-5P 221031-05-6P 221031-06-7P 221031-07-8P 221031-08-9P 221031-09-0P 221031-10-3P 221031-11-4P 221031-12-5P 221031-13-6P 221031-14-7P 221031-15-8P 221031-16-9P 221031-17-0P 221031-18-1P 221031-19-2P 221031-20-5P 221031-21-6P 221031-22-7P 221031-23-8P 221031-24-9P 221031-25-0P 221031-26-1P 221031-27-2P 221031-28-3P 221031-29-4P 221031-30-7P 221031-31-8P 221031-32-9P 221031-33-0P 221031-34-1P 221031-35-2P 221031-36-3P 221031-37-4P 221031-38-5P 221031-39-6P 221031-40-9P 221031-41-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

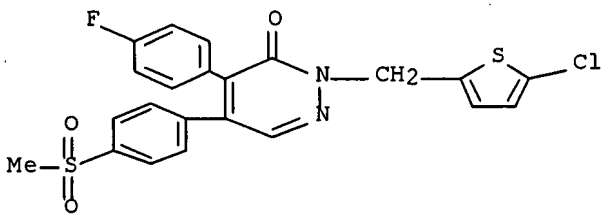
IT 221031-64-7P 221031-65-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

RETABLE

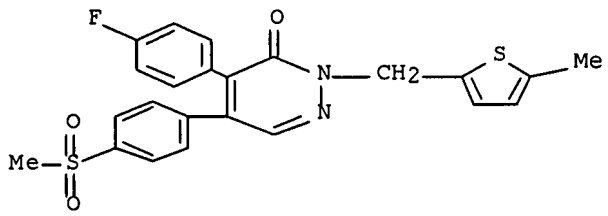
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
F Hoffmann-La Roche Ag	1996			EP 0714895 A	HCAPLUS
Griswold, D	1996	16	181	MEDICINAL RESEARCH R	HCAPLUS
Medicis Corporation	1988			WO 8809675 A	HCAPLUS
Rohm And Haas Company	1996			EP 0711759 A	HCAPLUS

IT **221025-73-6P 221025-74-7P 221025-98-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

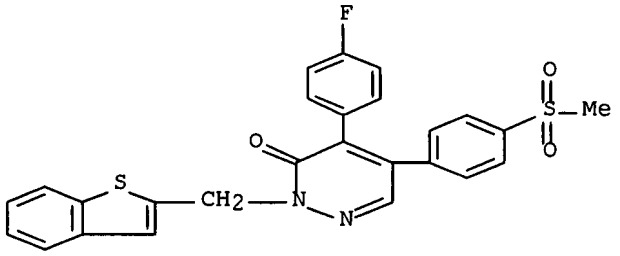
RN 221025-73-6 HCAPLUS
CN 3(2H)-Pyridazinone, 2-[(5-chloro-2-thienyl)methyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



RN 221025-74-7 HCAPLUS
CN 3(2H)-Pyridazinone, 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-2-[(5-methyl-2-thienyl)methyl]- (9CI) (CA INDEX NAME)



RN 221025-98-5 HCAPLUS
CN 3(2H)-Pyridazinone, 2-(benzo[b]thien-2-ylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



L99 ANSWER 11 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 11
ACCESSION NUMBER: 1994:435618 HCAPLUS Full-text
DOCUMENT NUMBER: 121:35618
TITLE: **Pyridazinone** derivatives and processes for preparing them
INVENTOR(S): Ishida, Akihoko; Homma, Koichi; Kono, Harumichi; Tamura, Koji; Sasaki, Yasuhiko
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 47 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
EP 579059	A1	19940119	EP 1993-110611		19930702	<--
EP 579059	B1	19990512				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE						
JP 06016663	A	19940125	JP 1992-215354		19920702	<--
CA 2099743	A1	19940103	CA 1993-2099743		19930629	<--
JP 06073020	A	19940315	JP 1993-159338		19930629	<--
AT 179972	T	19990515	AT 1993-110611		19930702	<--
US 5739132	A	19980414	US 1996-767444		19961216	<--
PRIORITY APPLN. INFO.:			JP 1992-215354	A	19920702	<--
			JP 1992-215355	A	19920702	<--
			US 1993-83489	B1	19930630	<--

OTHER SOURCE(S): MARPAT 121:35618
ED Entered STN: 23 Jul 1994
AB **Pyridazinones** I wherein (1) R1 is a substituted or unsubstituted C1-10 alkyl, a C3-6 cycloalkyl, a lower alkenyl, a heterocyclic group having N, O or S atom or camphor-10-yl; R3 is hydrogen, a substituted or unsubstituted lower alkyl or a lower alkenyl; or R1 and R3 are bonded at terminal ends thereof to form a lower alkylene; and Z is a group represented by II where n is 1 or 2; and D is hydrogen or a halogen; or (2) R1 is a substituted or unsubstituted C1-10 alkyl, a substituted or unsubstituted Ph, a C3-6 cycloalkyl, a lower alkenyl, a heterocyclic group having N, O or S atom or camphor-10-yl; R3 is hydrogen, a substituted or unsubstituted lower alkyl or a lower alkenyl; or R1 and R3 are bonded at terminal ends thereof to form a lower alkylene; and Z is a group represented by III and R2 is hydrogen, a substituted or unsubstituted lower alkyl, an aryl or a lower alkenyl; and -A-B- is an ethylene or vinylene each of which may be substituted by 1 or 2 groups selected from the group consisting of a lower alkyl and Ph group, or a pharmaceutically acceptable salt thereof were prepared and are useful for protecting from endotoxin shock and curing nephritis. Thus, mice treated with 2-methylsulfonylamino-5-[4,5-

dihydropyridazin -3(2H)-on-6-yl]indan (prepared by methanesulfonylation of 2-amino-5-[4,5- **dihydropyridazin**-3(2H)-on-6-yl]indan) had 100% survival rate vs. a control when infected with an endotoxin (lipopolysaccharide) derived from Escherichia coli.

IC ICM C07D237-04
ICS C07D237-14; C07D409-04; A61K031-50; C07D401-12; C07D409-12; C07D413-12; C07D417-12; C07D403-12; C07D409-06; C07D401-06; C07D403-06; C07D401-14

CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST **pyridazinone** prepn endotoxin shock nephritis

IT Shock
(endotoxin, **pyridazinones** for)

IT Kidney, disease
(nephritis, **pyridazinones** for treatment of)

IT 31952-21-3P 82985-09-9P 138993-85-8P 155719-25-8P 155719-31-6P
155719-32-7P 155719-33-8P 155719-35-0P 155719-36-1P 155719-37-2P
155719-41-8P 155719-43-0P 155719-50-9P 155719-51-0P 155719-52-1P
155719-53-2P 155719-54-3P 155719-60-1P 155719-62-3P 155719-63-4P
155719-64-5P 155719-66-7P 155719-67-8P 155719-68-9P 155719-69-0P
155719-70-3P 155719-71-4P 155719-72-5P 155719-73-6P 155719-74-7P
155719-75-8P 155719-76-9P 155719-77-0P 155719-78-1P 155719-79-2P
155719-80-5P 166978-75-2P 166978-76-3P 166978-77-4P 166978-78-5P
166978-85-4P 172680-14-7P 172680-41-0P 172680-79-4P 172680-80-7P
172680-81-8P 172680-82-9P 172680-83-0P 172680-85-2P 172680-87-4P
172680-88-5P 172680-89-6P 172680-90-9P 172680-91-0P 172680-92-1P
172680-93-2P 172680-94-3P 172680-99-8P 172681-00-4P 172681-01-5P
172681-02-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of **pyridazinones** for endotoxin shock protection and nephritis treatment)

IT 155718-08-4P 155718-23-3P 155718-25-5P 155718-27-7P 155718-33-5P
155718-34-6P 155718-38-0P 155718-49-3P 155718-66-4P 155718-74-4P
155718-80-2P 155718-89-1P 155718-90-4P 155718-92-6P 155719-08-7P
155719-09-8P 155719-10-1P 155719-11-2P 155719-12-3P 155719-13-4P
155719-14-5P 155719-15-6P 155719-16-7P 155719-17-8P 155719-18-9P
155719-19-0P 155719-20-3P 155719-21-4P 155719-22-5P 155719-23-6P
172679-62-8P 172679-63-9P 172679-64-0P 172679-65-1P 172679-66-2P
172679-67-3P 172679-68-4P 172679-69-5P 172679-70-8P 172679-71-9P
172679-72-0P 172679-73-1P 172679-74-2P 172679-75-3P 172679-76-4P
172679-77-5P 172679-78-6P 172679-79-7P 172679-80-0P 172679-81-1P
172679-82-2P 172679-83-3P 172679-84-4P 172679-85-5P 172679-86-6P
172679-88-8P 172679-92-4P 172679-93-5P 172679-94-6P 172679-95-7P
172679-96-8P 172679-97-9P 172680-00-1P 172680-01-2P 172680-02-3P
172680-03-4P 172680-04-5P 172680-05-6P 172680-06-7P 172680-07-8P
172680-08-9P 172680-11-4P 172680-12-5P 172680-13-6P 172680-15-8P
172680-16-9P 172680-17-0P 172680-18-1P 172680-19-2P 172680-20-5P
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172680-26-1P 172680-27-2P 172680-29-4P 172680-30-7P 172680-31-8P
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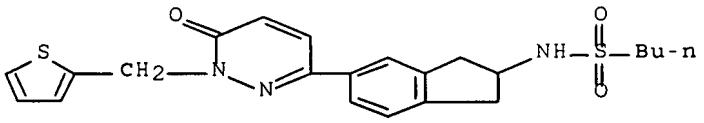
172680-38-5P 172680-39-6P 172680-40-9P 172680-42-1P 172680-43-2P
172680-44-3P 172680-45-4P 172680-46-5P **172680-47-6P**
172680-48-7P 172680-49-8P 172680-50-1P 172680-53-4P 172680-55-6P
172680-56-7P 172680-57-8P 172680-58-9P 172680-59-0P 172680-60-3P
172680-61-4P 172680-62-5P 172680-63-6P 172680-64-7P 172680-65-8P
172680-66-9P 172680-67-0P 172680-68-1P 172680-69-2P 172680-70-5P
172680-89-6P 172680-90-9P 172680-91-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for endotoxin shock protection and nephritis treatment)

IT 75-36-5, Acetyl chloride 75-77-4, Chlorotrimethylsilane, reactions 75-86-5 79-22-1, Methyl chlorocarbonate 79-30-1, 2-Methylpropionyl chloride 85-44-9, 1,3-Isobenzofurandione 98-09-9, Benzenesulfonyl chloride 100-39-0, Benzyl bromide 100-52-7, Benzaldehyde, reactions 103-80-0, Phenylacetyl chloride 105-36-2, Ethyl bromoacetate 107-08-4, Propyl iodide 108-30-5, reactions 124-63-0, Methanesulfonyl chloride 127-68-4 302-01-2, Hydrazine, reactions 407-25-0, Trifluoroacetic anhydride 617-86-7, Triethylsilane 754-03-0, Ethanesulfonyl fluoride 1490-25-1 1622-32-8 1633-82-5 2386-60-9, Butanesulfonyl chloride 2975-41-9, 2-Aminoindan 3099-31-8, 3-Picolyl chloride 3144-16-9, (+)-Camphorsulfonic acid 3878-55-5, Methyl hydrogen succinate 4584-46-7 16029-98-4 16629-19-9, 2-**Thiophenesulfonyl** chloride 114149-01-8 138006-38-9 155718-74-4 155719-08-7 155719-63-4 155719-80-5 155719-82-7 155719-85-0 155719-86-1 166978-75-2 172679-98-0 172680-34-1 172680-55-6 172680-56-7 172680-84-1 172680-86-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of **pyridazinones** for endotoxin shock protection and nephritis treatment)

IT **172680-47-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for endotoxin shock protection and nephritis treatment)

RN 172680-47-6 HCAPLUS

CN 1-Butanesulfonamide, N-[5-[1,6-dihydro-6-oxo-1-(2-thienylmethyl)-3-pyridazinyl]-2,3-dihydro-1H-inden-2-yl]- (9CI) (CA INDEX NAME)



L99 ANSWER 12 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 12

ACCESSION NUMBER: 1994:134401 HCAPLUS Full-text

DOCUMENT NUMBER: 120:134401

TITLE: Novel antiasthmatic agents with dual activities of thromboxane A2 synthetase inhibition and bronchodilation. 2. 4-(3-Pyridyl)-1(2H)-phthalazinones

AUTHOR(S): Yamaguchi, Masahisa; Kamei, Kenshi; Koga, Takaki; Akima, Michitaka; Maruyama, Akinori; Kuroki, Toshio; Ohi, Nobuhiro

CORPORATE SOURCE: Fuji-Gotemba Res. Lab., Chugai Pharm. Co., Ltd., Gotemba, 412, Japan

SOURCE: Journal of Medicinal Chemistry (**1993**), 36(25), 4061-8
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 19 Mar 1994

AB A series of novel 4-(3-pyridyl)-1(2H)-phthalazinone derivs. which possess dual activities of thromboxane A2 (TXA2) synthetase inhibition and bronchodilation was synthesized, and their pharmacol. activities were evaluated. While the length and the bulk of 2-alkyl substituents had no influence on either activity, the 2-substituents with polar groups reduced bronchodilatory activity. On introduction of heteroarom. nuclei into the 4-position of the phthalazinone I (R = 1-imidazolyl, R1 = Et) and I (R = 5-**thiazolyl**, R1 = Me,

Et) were as active as the parent I (R = 3-pyridyl, R1 = Et). These findings suggest that heteroarom. nuclei at the 4-position of phthalazinones play a critical role in TXA2 synthetase inhibition. Addnl., the hydrophobicity of the compds. was found to exert a marked influence on bronchodilatory activity. These observations led to the selection of 2-ethyl-4-(3-pyridyl)-1(2H)-phthalazinone (I, R = 3-pyridyl, R1 = Et) (KK-505) and 2-methyl-4-(5-**thiazolyl**)-1(2H)-phthalazinone (I, R = 5-**thiazolyl**, R1 = Me,) (KK-562) for further studies. Although their precise mechanism of action remains unclear, this series of novel phthalazinone derivs. represents a new class of antiasthma agents with dual activities.

CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 7

IT 75884-68-3P 137381-08-9P 137381-66-9P 137381-67-0P 137381-68-1P
137381-69-2P 137381-70-5P 137381-71-6P 137381-72-7P 137381-74-9P
137381-75-0P 137381-77-2P 137381-78-3P 137381-79-4P 137381-80-7P
137381-81-8P 137381-82-9P 137381-85-2P 137381-86-3P 137381-87-4P
137381-89-6P 137381-90-9P 137381-91-0P 137381-92-1P 137381-94-3P
137381-95-4P 137381-96-5P 137381-98-7P 137382-00-4P
137382-01-5P 137382-02-6P 137382-04-8P 137382-05-9P
137382-06-0P 137382-07-1P 137382-08-2P 137382-10-6P 137382-11-7P
137382-12-8P 137382-13-9P 137382-14-0P 137382-15-1P 137382-16-2P
137382-18-4P 137382-36-6P 153077-98-6P 153077-99-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and thromboxane A2 synthetase inhibition and bronchodilation activity of)

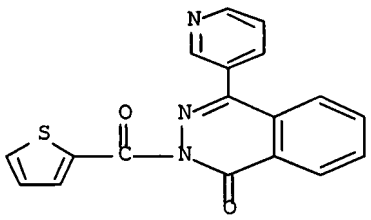
IT 108-98-5, Benzenethiol, reactions 288-94-8, 1H-Tetrazole 1450-85-7, 2-Pyrimidinethiol 25377-76-8, 2-**Thiazolinethiol**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (bromoethyl)phthalazinones)

IT 288-47-1, **Thiazole** 4595-59-9, 5-Bromopyrimidine 79265-30-8, 2-(Trimethylsilyl)**thiazole**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phthalic anhydride)

IT 85-44-9, Phthalic anhydride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with **thiazole**)

IT **137382-01-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and thromboxane A2 synthetase inhibition and bronchodilation activity of)

RN 137382-01-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3-pyridinyl)-2-(2-thienylcarbonyl)- (9CI) (CA INDEX NAME)



L99 ANSWER 13 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 13

ACCESSION NUMBER: 1992:83619 HCAPLUS Full-text
DOCUMENT NUMBER: 116:83619
TITLE: Potent, orally active aldose reductase inhibitors related to zopolrestat: surrogates for **benzothiazole** side chain
AUTHOR(S): Mylari, Banavara L.; Beyer, Thomas A.; Scott, Pamela J.; Aldinger, Charles E.; Dee, Michael F.; Siegel, Todd W.; Zembrowski, William J.
CORPORATE SOURCE: Cent. Res. Div., Pfizer Inc., Groton, CT, 06340, USA
SOURCE: Journal of Medicinal Chemistry (**1992**), 35(3), 457-65
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 06 Mar 1992

AB A broad structure-activity program was undertaken in search of effective surrogates for the key **benzothiazole** side chain of the potent aldose reductase inhibitor, zopolrestat. A structure-driven approach was pursued, which spanned exploration of three areas: (1) 5/6 fused heterocycles, such as benzoxazole, **benzothiophene**, benzofuran, and imidazopyridine; (2) 5-membered heterocycles, including oxadiazole, oxazole, **thiazole**, and thiadiazole, with pendant aryl groups, and (3) thioanilide as a formal equivalent of **benzothiazole.** Several benzoxazole- and 1,2,4-oxadiazole-derived analogs were found to be potent inhibitors of aldose reductase from human placenta and were orally active in preventing sorbitol accumulation in rat sciatic nerve, in an acute test of diabetic complications. Phthalazineacetic acid I was the best of the benzoxazole series ([C50 = 3.2 + 10-9M); it suppressed accumulation of sorbitol in rat sciatic nerve by 78% at an oral dose of 10 mg/kg. Oxadiazolyl derivative II with IC50 < 1.0 + 10-8M, caused a 69% reduction in sorbitol accumulation in rat sciatic nerve at an oral dose of 25 mg/kg. The thioanilide side chain features in III proved to be an effective surrogate for **benzothiazole.** III was highly potent in vitro (IC50 = 5.2 + 10-8M) but did not show oral activity when tested at 100 mg/kg. Addnl. structure-activity relationships encompassing a variety of heterocyclic side chains are discussed.

CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 110703-54-3P 110703-55-4P 110703-57-6P 110703-59-8P 110703-60-1P
110703-62-3P 110703-63-4P 110703-64-5P 110703-73-6P 110703-74-7P
110703-77-0P **110703-78-1P** 110721-48-7P 110722-35-5P
110722-36-6P 110722-45-7P 110722-46-8P 110749-07-0P 110749-08-1P
112065-65-3P **124168-21-4P** 131337-23-0P 131337-24-1P
131337-27-4P 131337-28-5P 131337-29-6P 131337-32-1P 131337-33-2P
131337-35-4P **131337-37-6P** **131337-38-7P**
138129-12-1P 138129-13-2P 138129-14-3P 138129-29-0P 138129-30-3P
138129-31-4P 138129-32-5P 138129-33-6P 138129-34-7P 138129-35-8P
138129-36-9P 138129-37-0P 138129-38-1P 138129-39-2P 138129-40-5P
138129-41-6P 138129-42-7P 138129-43-8P 138129-44-9P 138151-14-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and aldose reductase inhibition of)

IT 110703-66-7P 110703-79-2P 110703-80-5P 110703-81-6P 110703-83-8P
110703-87-2P 110703-88-3P 110703-91-8P **110703-92-9P**
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110722-38-8P 110722-39-9P 110722-41-3P 110722-43-5P 110722-44-6P
110749-09-2P **124168-24-7P** 131337-22-9P 131337-26-3P
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138128-94-6P **138128-95-7P** **138128-96-8P** 138128-97-9P
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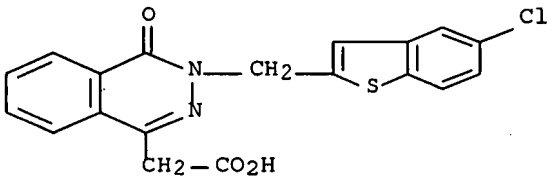
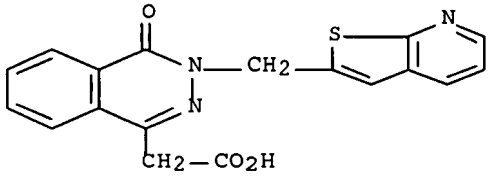
138129-22-3P 138129-23-4P 138129-24-5P 138129-25-6P 138129-26-7P
138129-27-8P 138129-28-9P 138151-13-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT **110703-78-1P 124168-21-4P 131337-35-4P**
131337-37-6P 131337-38-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and aldose reductase inhibition of)

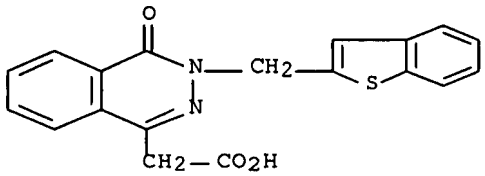
RN 110703-78-1 HCAPLUS
CN 1-Phthalazineacetic acid, 3-[(5-chlorobenzo[b]thien-2-yl)methyl]-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



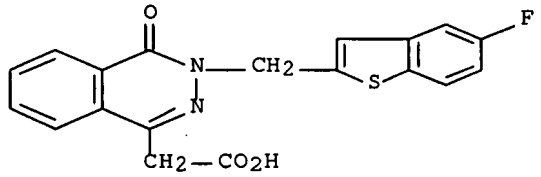
RN 124168-21-4 HCAPLUS
CN 1-Phthalazineacetic acid, 3,4-dihydro-4-oxo-3-(thieno[2,3-b]pyridin-2-ylmethyl)- (9CI) (CA INDEX NAME)



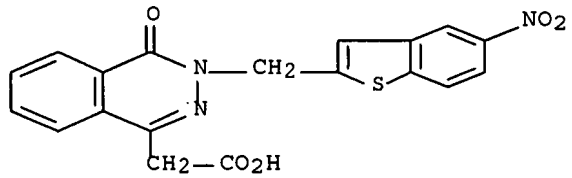
RN 131337-35-4 HCAPLUS
CN 1-Phthalazineacetic acid, 3-(benzo[b]thien-2-ylmethyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



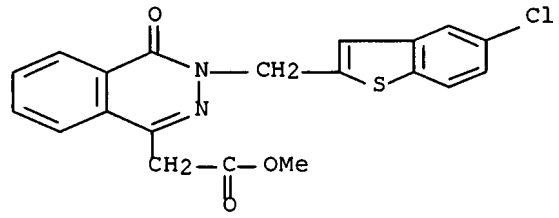
RN 131337-37-6 HCAPLUS
CN 1-Phthalazineacetic acid, 3-[(5-fluorobenzo[b]thien-2-yl)methyl]-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



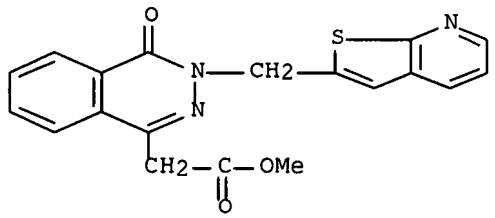
RN 131337-38-7 HCAPLUS
CN 1-Phthalazineacetic acid, 3,4-dihydro-3-[(5-nitrobenzo[b]thien-2-yl)methyl]-4-oxo- (9CI) (CA INDEX NAME)



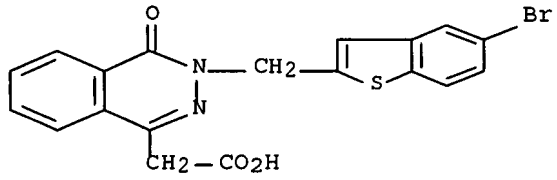
IT **110703-92-9P 124168-24-7P 131337-39-8P 131337-40-1P 131337-48-9P 138128-95-7P 138128-96-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 110703-92-9 HCAPLUS
CN 1-Phthalazineacetic acid, 3-[(5-chlorobenzo[b]thien-2-yl)methyl]-3,4-dihydro-4-oxo-, methyl ester (9CI) (CA INDEX NAME)



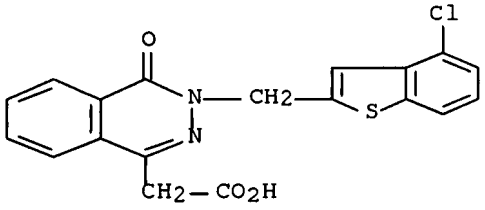
RN 124168-24-7 HCAPLUS
CN 1-Phthalazineacetic acid, 3,4-dihydro-4-oxo-3-(thieno[2,3-b]pyridin-2-ylmethyl)-, methyl ester (9CI) (CA INDEX NAME)



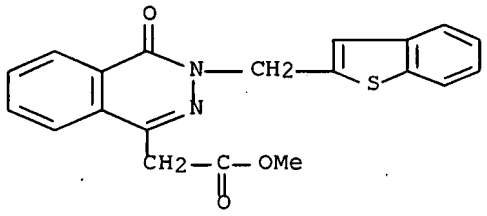
RN 131337-39-8 HCAPLUS
CN 1-Phthalazineacetic acid, 3-[(5-bromobenzo[b]thien-2-yl)methyl]-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



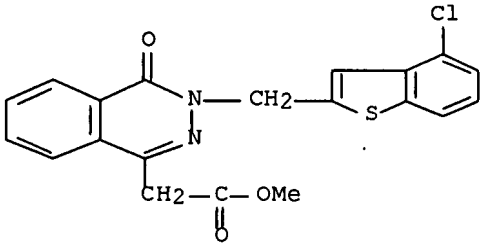
RN 131337-40-1 HCAPLUS
CN 1-Phthalazineacetic acid, 3-[(4-chlorobenzo[b]thien-2-yl)methyl]-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



RN 131337-48-9 HCAPLUS
CN 1-Phthalazineacetic acid, 3-(benzo[b]thien-2-ylmethyl)-3,4-dihydro-4-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 138128-95-7 HCAPLUS
CN 1-Phthalazineacetic acid, 3-[(4-chlorobenzo[b]thien-2-yl)methyl]-3,4-dihydro-4-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 138128-96-8 HCAPLUS
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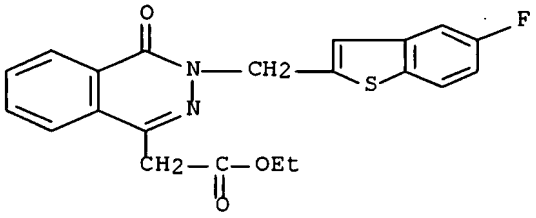

L99 ANSWER 14 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:205961 HCAPLUS Full-text
DOCUMENT NUMBER: 142:197900
TITLE: Product class 10: phthalazines
AUTHOR(S): Haider, N.; Holzer, W.
CORPORATE SOURCE: Germany
SOURCE: Science of Synthesis (2004), 16, 315-372
CODEN: SSCYJ9
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
ED Entered STN: 15 Mar 2004
AB A review. Preparation is given for phthalazines via ring closure or transformation reactions, aromatization or substituent modification.
CC 28-0 (Heterocyclic Compounds (More Than One Hetero Atom))
IT 50-00-0, Formaldehyde, reactions 57-13-6, Urea, reactions 57-56-7, Hydrazinecarboxamide 60-34-4 62-53-3, Benzenamine, reactions 64-19-7, Acetic acid, reactions 67-62-9 70-11-1 71-43-2, Benzene, reactions 74-89-5, Methanamine, reactions 75-07-0, Acetaldehyde, reactions 75-16-1 75-24-1 77-78-1 79-19-6, Hydrazinecarbothioamide 79-22-1 84-58-2 85-44-9, 1,3-Isobenzofurandione 85-52-9 88-99-3, 1,2-Benzenedicarboxylic acid, reactions 89-74-7 91-15-6, 1,2-Benzenedicarbonitrile 93-60-7 93-98-1 95-47-6, reactions 95-76-1 98-01-1, 2-Furancarboxaldehyde, reactions 98-03-3, 2-**Thiophenecarboxaldehyde** 98-09-9, Benzenesulfonyl chloride

98-80-6 98-88-4, Benzoyl chloride 100-44-7, reactions 100-52-7, Benzaldehyde, reactions 100-61-8, reactions 100-63-0 104-87-0 104-88-1, reactions 105-36-2 105-39-5 105-53-3 105-56-6 106-42-3, reactions 106-47-8, reactions 107-13-1, 2-Propenenitrile, reactions 107-14-2 108-24-7 108-38-3, reactions 108-88-3, reactions 108-95-2, Phenol, reactions 109-01-3 109-65-9 109-72-8, reactions 109-73-9, 1-Butanamine, reactions 109-77-3, Propanedinitrile 109-84-2 110-18-9 110-46-3 113-00-8, Guanidine 118-92-3 119-67-5 120-14-9 120-57-0, 1,3-Benzodioxole-5-carboxaldehyde 121-69-7, reactions 123-11-5, reactions 123-75-1, Pyrrolidine, reactions 128-08-5 140-29-4, Benzeneacetonitrile 141-43-5, reactions 334-88-3 368-39-8 368-78-5 420-04-2, Cyanamide 462-80-6, 1,3-Cyclohexadien-5-yne 479-87-8 480-91-1 536-40-3 555-96-4 577-56-0 589-21-9 591-50-4 603-11-2 610-93-5 613-94-5 623-73-4 637-80-9 641-63-4 642-27-3 643-79-8, 1,2-Benzenedicarboxaldehyde 652-40-4 670-80-4 704-00-7 762-42-5 824-79-3 865-47-4 917-54-4 936-52-7 942-81-4 1122-91-4 1125-99-1 1129-28-8 1159-86-0 1530-45-6 1576-35-8 1673-47-8 1679-18-1 1766-63-8 1875-48-5 1885-14-9 1997-41-7 2142-73-6 2148-30-3 2166-14-5 2181-42-2 2258-87-9 2311-91-3 2360-45-4 2368-80-1 2417-72-3 2417-73-4 2435-53-2 2459-07-6 2459-09-8 2684-62-0 2741-57-3 2969-81-5 3260-44-4 3291-03-0 3468-11-9 3598-13-8 3598-14-9 3619-22-5 3900-89-8 3958-79-0 4114-31-2 4176-69-6 4333-62-4 4333-65-7 4445-58-3, [1,1'-Biphenyl]-3,4-dicarboxylic acid 4521-61-3 4540-16-3 4821-94-7 4870-65-9 5004-42-2 5271-67-0, 2-**Thiophenecarbonyl** chloride 5720-05-8 5720-06-9 5720-07-0 5814-05-1 5999-20-2 6118-66-7 6781-29-9 6830-78-0 6833-23-4 7087-68-5 7112-37-0 7148-07-4 7464-91-7 7465-88-5 7477-28-3 7658-80-2 7677-24-9 7681-11-0, Potassium iodide (KI), reactions 7694-81-7, 1-Phthalazinecarbonitrile 10034-85-2, Hydriodic acid 10251-20-4 10365-98-7 10478-89-4 10478-99-6 13050-47-0 13209-15-9 13746-66-2 14092-11-6 14352-51-3 14660-52-7 14671-41-1 15994-77-1 16675-55-1 16721-80-5, Sodium sulfide (Na(SH)) 17082-09-6 17127-13-8 17933-03-8 18138-18-6 18496-19-0 18584-63-9 19064-68-7 19172-47-5 19641-29-3 20277-69-4 21343-93-1 21950-75-4 22446-12-4 23952-05-8 24280-34-0 24826-74-2 25641-99-0 25732-35-8 27693-49-8 29360-77-8 32003-14-8 33027-12-2 33133-69-6 33901-44-9 33901-46-1 34613-09-7 37074-38-7 39519-78-3 39830-63-2 42760-46-3 42833-31-8 43073-12-7 43111-31-5 43111-32-6 46496-80-4 50635-21-7 50635-22-8 50635-23-9 52010-22-7 52044-75-4 52302-45-1, 1,3-Benzodioxole-5,6-dicarboxaldehyde 54109-03-4 56107-12-1 56107-13-2 56611-61-1 57901-54-9 58268-28-3 61503-68-2 63503-60-6 63536-24-3 63536-25-4 63536-26-5 63536-27-6 63536-28-7 64019-77-8 64779-60-8 65095-33-2 65237-17-4 65489-47-6 66645-91-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of phthalazines)

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RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of phthalazines)

RETABLE

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Druey, J	1967	7	223	Med Chem (New York)	HCAPLUS
Dunet, A	1948		1081	Bull Soc Chim Fr	HCAPLUS
D'Amico, J	1968			US 3379700	HCAPLUS
Eguchi, Y	1991	39	1846	Chem Pharm Bull	HCAPLUS
Eguchi, Y	1991	39	2009	Chem Pharm Bull	HCAPLUS
Eguchi, Y	1991	39	795	Chem Pharm Bull	HCAPLUS
Eicher, T	1980	113	424	Chem Ber	HCAPLUS
El-Feky, S	1991	65	1645	Pol J Chem	HCAPLUS
El-Hashash, M	1995	40	173	Rev Roum Chim	HCAPLUS
El-Safty, M	1991	36	187	Rev Roum Chim	HCAPLUS
El-Sharief, A	1983	22	87	Indian J Chem, Sect	
Elderfield, R	1957	6	186	Heterocyclic Compoun	
Elslager, E	1968	5	609	J Heterocycl Chem	HCAPLUS
Elvidge, J	1960		1710	J Chem Soc	HCAPLUS
Engel, J	1994			EP 590551	HCAPLUS
Ephraim, J	1893	26	1376	Ber Dtsch Chem Ges	
Escudero, F	1983		1735	J Chem Soc, Perkin T	HCAPLUS
Ezquerra, J	1988	25	917	J Heterocycl Chem	HCAPLUS
Favini, G	1958	8	60	Nuovo Cimento	HCAPLUS
Fieser, L	1967	1	892	Reagents for Organic	
Fischer, G	1995	198	183	Chem Phys	HCAPLUS
Flitsch, W	1967	79	141	Angew Chem	
Flitsch, W	1967	6	173	Angew Chem Int Ed En	HCAPLUS
Flitsch, W	1969	102	1304	Chem Ber	HCAPLUS
Francis, J	1982	60	1214	Can J Chem	HCAPLUS
Fujii, K	1956	1	1	Annu Rep G Tanabe Co	HCAPLUS
Fujii, K	1956	1	3	Annu Rep G Tanabe Co	HCAPLUS
Gabriel, S	1893	26	2210	Ber Dtsch Chem Ges	
Gabriel, S	1893	26	521	Ber Dtsch Chem Ges	
Gabriel, S	1893	26	705	Ber Dtsch Chem Ges	
Gabriel, S	1895	28	1830	Ber Dtsch Chem Ges	
Gabriel, S	1897	30	3022	Ber Dtsch Chem Ges	
Gabriel, S	1903	36	3373	Ber Dtsch Chem Ges	HCAPLUS
Gautheron-Chapoulaud, V	1999	55	5389	Tetrahedron	
Gawer, A	1965	42	2658	J Chem Phys	HCAPLUS
Gillies, I	1996	37	4065	Tetrahedron Lett	HCAPLUS
Girardot, M	1998	63	10063	J Org Chem	HCAPLUS
Goldschmidt, S	1961	94	169	Chem Ber	HCAPLUS
Gompper, R	1960	93	198	Chem Ber	HCAPLUS
Gottlieb, J	1899	32	958	Ber Dtsch Chem Ges	
Gould, K	1980		1834	J Chem Soc, Perkin T	HCAPLUS
Grasso, S	2000	43	2851	J Med Chem	HCAPLUS
Guery, S	2001		699	Synthesis	HCAPLUS
Guingant, A	1975		2246	Bull Soc Chim Fr	HCAPLUS
Gundermann, K	1962	95	2018	Chem Ber	HCAPLUS
Gundermann, K	1969	102	3241	Chem Ber	HCAPLUS
Gundermann, K	1965	684	127	Justus Liebigs Ann C	HCAPLUS

Haider, N	1999	332	408	Arch Pharm (Weinheim	HCAPLUS
Haider, N	1995	41	2519	Heterocycles	HCAPLUS
Haider, N	1994	31	357	J Heterocycl Chem	HCAPLUS
Haider, N	1996	64	399	Sci Pharm	HCAPLUS
Haider, N	1999	29	1577	Synth Commun	HCAPLUS
Haider, N	1991	47	3959	Tetrahedron	HCAPLUS
Hameka, H	1958	1	9	Mol Phys	
Hanasato, N	1999	277	L225	Am J Physiol	HCAPLUS
Harling, J	1998			WO 9846574	HCAPLUS
Hartmann, M	1949			US 2484029	HCAPLUS
Harvey, R	1978	43	3423	J Org Chem	HCAPLUS
Hatzelmann, A	1999			EP 934933	HCAPLUS
Hatzelmann, A	1999			WO 9931071	HCAPLUS
Haworth, R	1948		777	J Chem Soc	HCAPLUS
Hayashi, B	1968	88	83	Yakugaku Zasshi	HCAPLUS
Hayashi, E	1977	25	579	Chem Pharm Bull	HCAPLUS
Hayashi, E	1962	82	584	Yakugaku Zasshi	HCAPLUS
Hayashi, E	1966	86	576	Yakugaku Zasshi	HCAPLUS
Hayashi, E	1967	87	807	Yakugaku Zasshi	HCAPLUS
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Hayashi, E	1968	88	1333	Yakugaku Zasshi	HCAPLUS
Hayashi, T	1995			EP 652213	HCAPLUS
Helberger, J	1937	531	279	Justus Liebigs Ann C	HCAPLUS
Henriques, R	1888	21	1607	Ber Dtsch Chem Ges	
Hirsch, A	1965	43	2708	Can J Chem	HCAPLUS
Hirsch, A	1966	44	1551	Can J Chem	HCAPLUS
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Hirsch, A	1965	2	206	J Heterocycl Chem	HCAPLUS
Hirsch, A	1966	3	38	J Heterocycl Chem	HCAPLUS
Hirt, R	1956	25	574	J Chem Phys	HCAPLUS
Horn, H	1990	45	724	Pharmazie	HCAPLUS
Hosomi, A	1987	52	4423	J Org Chem	HCAPLUS
Huiszoon, C	1972	28	3415	Acta Crystallogr, Se	HCAPLUS
Hunston, R	1989	IV	114	Rodd's Chemistry of	
Ikeda, T	1957	7	6	Kanazawa Daigaku Yak	HCAPLUS
Ikeda, T	1958	8	1	Kanazawa Daigaku Yak	HCAPLUS
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Inoue, M	1973			DE 2237832	HCAPLUS
Ishikawa, M	1991			JP 03048664	HCAPLUS
Ishikawa, M	1980	28	2770	Chem Pharm Bull	HCAPLUS
Ishikawa, M	1981	16	25	Heterocycles	HCAPLUS
Islam, A	1980	22	209	Egypt J Chem	
Islam, A	1978	16	50	Indian J Chem, Sect	
Ismail, M	1991	128	251	Acta Chim Hung	HCAPLUS
Ismail, M	1995	36	479	Egypt J Chem	
Ismail, M	1985	327	177	J Prakt Chem	HCAPLUS
Ismail, M	1984	40	2983	Tetrahedron	HCAPLUS
Iwamoto, K	1995	43	679	Chem Pharm Bull	HCAPLUS
Jahine, H	1978	16	689	Indian J Chem, Sect	
Joshi, H	1990	67	779	J Indian Chem Soc	HCAPLUS
Kanahara, S	1964	84	483	Yakugaku Zasshi	HCAPLUS
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Kandile, N	1989	126	533	Acta Chim Hung	HCAPLUS
Kant, J	1985	22	1065	J Heterocycl Chem	HCAPLUS
Katritzky, A	1963	1	365	Adv Heterocycl Chem	
Knaack, M	1996		1477	Liebigs Ann	HCAPLUS
Kodama, K	1999	290	748	J Pharmacol Exp Ther	HCAPLUS
Koehler, W	1967	100	1073	Chem Ber	HCAPLUS

Kolesnikov, V	1967	2	250	Chim Ther	HCAPLUS
Kondo, Y	1980		911	J Chem Soc, Perkin T	HCAPLUS
Kormendy, K	1979	102	39	Acta Chim Acad Sci H	HCAPLUS
Kormendy, K	1981	108	167	Acta Chim Acad Sci H	HCAPLUS
Kormendy, K	1984	117	363	Acta Chim Hung	HCAPLUS
Kormendy, K	1988	125	99	Acta Chim Hung	HCAPLUS
Kornet, M	1999	36	1095	J Heterocycl Chem	HCAPLUS
Kost, A	1967	1	43	Khim-Farm Zh	HCAPLUS
Kumada, S	1958	30	635	Yakugaku Kenkyo	HCAPLUS
Kundu, S	2002		823	Synlett	HCAPLUS
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Lieck, A	1905	38	3918	Ber Dtsch Chem Ges	
Long, S	1981	44	355	J Magn Reson	HCAPLUS
Longuet-Higgins, H	1949		971	J Chem Soc	
L'Vova, N	1980	16	1998	J Org Chem USSR (Eng	
L'Vova, N	1980	16	2340	Zh Org Khim	HCAPLUS
Machado, H	1995	339	255	THEOCHEM	HCAPLUS
Mahanti, M	1977	15	168	Indian J Chem, Sect	
Malikowski, T	1979			PL 100002	HCAPLUS
Marxer, A	1969	52	1376	Helv Chim Acta	HCAPLUS
Mason, S	1957		4874	J Chem Soc	HCAPLUS
Matsumoto, I	1973			JP 48044284	HCAPLUS
Matyus, P	1994	327	543	Arch Pharm (Weinheim	HCAPLUS
Merchant, J	1980	19	914	Indian J Chem, Sect	
Mitchell, R	1970	36	310	J Mol Spectrosc	HCAPLUS
Miyashita, A	1998	49	405	Heterocycles	HCAPLUS
Mizuno, Y	1954	2	225	Pharm Bull (Jpn)	HCAPLUS
Mohamed, F	1994	33	769	Indian J Chem, Sect	
Mokrosz, J	1996	31	973	Eur J Med Chem	HCAPLUS
Morgan, D	2000	56	5523	Tetrahedron	HCAPLUS
Mori, K	1962	82	1161	Yakugaku Zasshi	HCAPLUS
Moskovits, M	1984	88	5526	J Phys Chem	HCAPLUS
Muller, A	1954	19	1533	J Org Chem	HCAPLUS
Murgich, J	1992	96	9198	J Phys Chem	HCAPLUS
Mustafa, A	1960	82	2735	J Am Chem Soc	
Mustafa, A	1964	20	531	Tetrahedron	HCAPLUS
Mylari, B	1991	34	108	J Med Chem	HCAPLUS
Mylari, B	1991	56	2587	J Org Chem	HCAPLUS
Nada, A	2000	156	213	Phophorus, Sulfur Si	HCAPLUS
Nakajima, T	1958	55	793	J Chim Phys	HCAPLUS
Nanya, S	1995	32	1299	J Heterocycl Chem	HCAPLUS
Napoletano, M	2000			WO 0005218	HCAPLUS
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Napoletano, M	2000	10	2235	Bioorg Med Chem Lett	HCAPLUS
Napoletano, M	2001	11	33	Bioorg Med Chem Lett	HCAPLUS
Negm, A	1995	106	1	Phosphorus, Sulfur S	HCAPLUS
Nguyen Minh, T	1990	55	6177	J Org Chem	
Nielsen, J	1996	37	3351	Tetrahedron Lett	HCAPLUS
Nomoto, Y	1990	38	2179	Chem Pharm Bull	HCAPLUS
Occelli, E	1989	44	29	Farmaco	HCAPLUS
Oishi, E	1969	89	959	Yakugaku Zasshi	HCAPLUS
Oparin, D	1992	28	843	J Org Chem USSR (Eng	
Oparin, D	1992	28	7079	Zh Org Khim	HCAPLUS
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Otsuki, J	1997	70	671	Bull Chem Soc Jpn	HCAPLUS
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Parsons, P	1964	17	491	Aust J Chem	HCAPLUS
Patankar, J	1996	5	239	Indian J Heterocycl	HCAPLUS
Patel, N	1973	27	324	The Chemistry of Het	
Patel, N	1973	27	343	The Chemistry of Het	
Paul, V	1899	32	2014	Ber Dtsch Chem Ges	
Pei, X	1999	9	539	Bioorg Med Chem Lett	HCAPLUS
Pelletier, J	1996	39	343	J Med Chem	HCAPLUS
Perreault, H	1992	27	89	Org Mass Spectrom	HCAPLUS
Peters, A	1948		597	J Chem Soc	HCAPLUS
Pill, T	1995			DE 4333761	HCAPLUS
Popp, F	1967		59	Chem Commun	HCAPLUS
Popp, F	1968	5	879	J Heterocycl Chem	HCAPLUS
Potts, K	1969	34	3221	J Org Chem	HCAPLUS
Potts, K	1985	50	1677	J Org Chem	HCAPLUS
Prager, R	1982	18	327	Heterocycles	HCAPLUS
Pugmire, R	1969	91	6381	J Am Chem Soc	HCAPLUS
Racine, S	1887	239	78	Justus Liebigs Ann C	
Radl, S	1999	332	208	Arch Pharm (Weinheim	HCAPLUS
Ramage, G	1959	IV	1238	Rodd's Chemistry of	
Redemann, C	1949	29	78	Org Synth	HCAPLUS
Ried, W	1959	46	142	Naturwissenschaften	HCAPLUS
Rival, Y	1998	41	311	J Med Chem	HCAPLUS
Robev, S	1990	43	53	Dokl Bolg Akad Nauk	HCAPLUS
Robev, S	1990	43	65	Dokl Bolg Akad Nauk	HCAPLUS
Robev, S	1992	45	13	Dokl Bolg Akad Nauk	HCAPLUS
Rodda, H	1956		3509	J Chem Soc	HCAPLUS
Roser, W	1885	18	802	Ber Dtsch Chem Ges	
Rosseels, G	1965	74	91	Bull Soc Chim Belg	HCAPLUS
Rowe, F	1931		1918	J Chem Soc	HCAPLUS
Rowe, F	1933		1331	J Chem Soc	HCAPLUS
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Ruiz, A	1997	38	6205	Tetrahedron Lett	HCAPLUS
Ruxer, J	1995	32	643	J Heterocycl Chem	HCAPLUS
Sato, R	1990	63	1160	Bull Chem Soc Jpn	HCAPLUS
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Sayed, M	1991	9	45	Chin J Chem	HCAPLUS
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Schmidt, M	1992			DE 298996	HCAPLUS
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Shaikh, I	1986	29	1329	J Med Chem	HCAPLUS
Sharpless, K	1992	57	2768	J Org Chem	HCAPLUS
Shashikanth, S	1999	29	3503	Synth Commun	HCAPLUS
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Shatalov, G	1980		394	Khim Geterotsikl Soe	HCAPLUS
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Shevchenko, V	1986	22	711	Zh Org Chim	HCAPLUS
Shimizu, H	1982	104	7059	J Am Chem Soc	HCAPLUS
Simpson, J	1953	5	69	The Chemistry of Het	
Singh, J	1983	22	1083	Indian J Chem, Sect	
Smith, R	1962	27	879	J Org Chem	HCAPLUS
Soliman, F	1994	39	827	Rev Roum Chim	HCAPLUS
Somogyi, L	1985		1679	Liebigs Ann Chem	HCAPLUS
Srinivasan, V	1999	64	5644	J Org Chem	HCAPLUS
Staedeli, W	1980	63	504	Helv Chim Acta	HCAPLUS
Steffen, K	1973			DE 2153693	HCAPLUS
Stephenson, E	1957		174	Chem Ind (London)	HCAPLUS

Stephenson, E	1963		1913	J Chem Soc	HCAPLUS
Stolle, R	1932	135	128	J Prakt Chem	HCAPLUS
Strappaghetti, G	1998	33	501	Eur J Med Chem	HCAPLUS
Strappaghetti, G	2000	35	773	Eur J Med Chem	HCAPLUS
Suarez, M	1998	120	9526	J Am Chem Soc	HCAPLUS
Sugahara, M	1997	45	719	Chem Pharm Bull	HCAPLUS
Sugimoto, A	1985	33	2809	Chem Pharm Bull	HCAPLUS
Suzuki, Y	1998	46	199	Chem Pharm Bull	HCAPLUS
Taft, R	1986	108	3237	J Am Chem Soc	HCAPLUS
Takahashi, M	1987	91	5940	J Phys Chem	HCAPLUS
Takeuchi, I	1990	38	1504	Chem Pharm Bull	HCAPLUS
Tamborski, C	1985	28	139	J Fluorine Chem	HCAPLUS
Tarzia, G	1989	44	17	Farmaco	HCAPLUS
Tarzia, G	1989	44	3	Farmaco	HCAPLUS
Thomas, T	1985			EP 164593	HCAPLUS
Tisler, M	1984	3	1	Comprehensive Hetero	
Togo, H	1993		2417	J Chem Soc, Perkin T	HCAPLUS
Togo, H	1991	32	6559	Tetrahedron Lett	HCAPLUS
Tori, K	1963	11	681	Chem Pharm Bull	HCAPLUS
Treibs, W	1951	574	54	Justus Liebigs Ann C	HCAPLUS
Ueda, Y	1996			JP 08092244	HCAPLUS
Ueno, K	1972			DE 2145359	HCAPLUS
Uff, B	1977	6	1789	Heterocycles	HCAPLUS
Uff, B	1986		206	J Chem Res, Synop	HCAPLUS
Uff, B	1989		24	J Chem Res, Synop	HCAPLUS
Ukita, T	1996			EP 748805	HCAPLUS
Ukita, T	1998			JP 10226647	HCAPLUS
Ukita, T	1999	42	1088	J Med Chem	HCAPLUS
Van de Weijer, P	1976	8	187	Org Magn Reson	HCAPLUS
van der Zanden, J	1955	74	52	Recl Trav Chim Pays-	HCAPLUS
Vantorex Ltd	1967			NL 6609718	HCAPLUS
Vasilevskii, S	1985		1367	Izv Akad Nauk SSSR,	HCAPLUS
Vaughan, W	1946	68	1314	J Am Chem Soc	HCAPLUS
Vogelsang, D	1972			DE 2164058	HCAPLUS
Volynets, N	1982	18	1342	J Org Chem USSR (Eng	
Volynets, N	1982	18	1533	Zh Org Khim	HCAPLUS
von Rothenburg, R	1895	51	147	J Prakt Chem	
Wagner, G	1966	299	768	Arch Pharm (Weinheim	HCAPLUS
Wait, S	1966	19	25	J Mol Spectrosc	HCAPLUS
Warner, C	1962		1282	J Chem Soc	HCAPLUS
Watanabe, N	1996			WO 9605176	HCAPLUS
Watanabe, N	1998			WO 9807430	HCAPLUS
Watanabe, N	1999			WO 9942452	HCAPLUS
Watanabe, N	1998	41	3367	J Med Chem	HCAPLUS
Watanabe, N	2000	43	2523	J Med Chem	HCAPLUS
Werner, U	1994	41	99	Agents Actions	HCAPLUS
Wharton, C	1985		809	J Chem Soc, Perkin T	HCAPLUS
Witanowski, M	1981	16	309	Org Magn Reson	HCAPLUS
Woelbling, H	1905	38	3926	Ber Dtsch Chem Ges	
Wolf, W	1956			DE 941845	HCAPLUS
Woon, T	1986		2381	J Chem Soc, Dalton T	HCAPLUS
Xu, W	1998	8	1089	Bioorg Med Chem Lett	HCAPLUS
Yakovlev, S	1988	24	2159	J Org Chem USSR (Eng	
Yakovlev, S	1988	24	2433	Zh Org Khim	HCAPLUS
Yale, H	1953	75	675	J Am Chem Soc	HCAPLUS
Yamada, T	1982	25	975	J Med Chem	HCAPLUS
Yamaguchi, M	1993	36	4052	J Med Chem	HCAPLUS
Yamaguchi, M	1993	36	4061	J Med Chem	HCAPLUS
Zajac, W	1966	44	833	Can J Chem	HCAPLUS
Zellner, C	1936	58	1811	J Am Chem Soc	HCAPLUS

Zerweck, W	1956			DE 952810	HCAPLUS
Zerweck, W	1957			US 2786839	HCAPLUS
Zhang, D	1995	12	24	Guangpu Shiyanshi	HCAPLUS
Zhou, J	2000	37	1165	J Heterocycl Chem	HCAPLUS
Zugravescu, I	1968	14	51	An Stiint Univ Al I	HCAPLUS
Zugravescu, I	1962	7	1405	Rev Chim, Acad Rep P	HCAPLUS

IT **137382-01-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of phthalazines)
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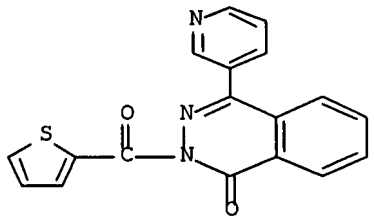

L99 ANSWER 15 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:489233 HCAPLUS Full-text
DOCUMENT NUMBER: 135:92640
TITLE: Preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain
INVENTOR(S): Brown, Dean Gordon; Bare, Thomas Michael; Murphy, Megan; Urbanek, Rebecca Ann; Xiao, Wenhua; McLaren, Frances Marie; Horchler, Carey Lynn
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 40 pp.
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LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047524	A1	20010705	WO 2000-SE2608	20001219 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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EP 1244453	A1	20021002	EP 2000-987933	20001219 <--
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JP 2003518500	T	20030610	JP 2001-548118		20001219 <--
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ZA 2002004781	A	20030915	ZA 2002-4781		20020613 <--
US 2003153571	A1	20030814	US 2002-168757		20021217 <--
PRIORITY APPLN. INFO.:			US 1999-171906P	P	19991223 <--
			US 2000-236785P	P	20000929 <--
			US 2000-236783P	P	20000929 <--
			EP 2000-987935	A3	20001219 <--
			WO 2000-SE2608	W	20001219 <--

OTHER SOURCE(S): MARPAT 135:92640
ED Entered STN: 06 Jul 2001
AB The title compds. [I; R1 = halo; A = CHR2(CH2)n (n = 0-2); R2 = alkyl; D = (un)substituted 5-6 membered heteroaryl or its benz-derivative having 1-3 ring atoms selected from N, O or S], useful for the treatment of pain, were prepared E.g., a multi-step synthesis of I.MeSO3H [R1 = 7-Cl; A = CHMe; D = 3-pyridyl] which showed Ki of 272 nM against binding to NMDA receptor glycine site, was given.
IC ICM A61K031-5025
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
ST **pyridazinoquinolinedione** prepn analgesic NMDA receptor glycine site
IT Glutamate receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(NMDA-binding, glycine site; preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)
IT Analgesics
(preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)
IT 349111-62-2P 349111-64-4P 349111-66-6P 349111-68-8P 349111-70-2P 349111-72-4P 349111-73-5P 349111-75-7P 349111-77-9P 349111-79-1P 349111-81-5P 349111-83-7P 349111-85-9P 349111-87-1P 349111-88-2P 349111-89-3P 349111-90-6P 349111-91-7P **349111-92-8P** **349111-93-9P** **349111-94-0P** **349111-95-1P** 349111-96-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)
IT 75-26-3, 2-Bromopropane 88-15-3, 2-**Acetylthiophene** 100-48-1, 4-Cyanopyridine 100-70-9, 2-Cyanopyridine 106-94-5, 1-Bromopropane 123-75-1, Pyrrolidine, reactions 350-03-8, 3-Acetylpyridine 762-42-5, Dimethyl acetylenedicarboxylate 870-46-2, tert-Butyl carbazate 872-85-5, 4-Pyridinecarboxaldehyde 926-62-5, Isobutylmagnesium bromide 1122-54-9, 4-Acetylpyridine 1192-62-7, 2-Acetylfuran 1570-48-5, 1-(3-Pyridyl)propan-1-one 1646-26-0, Benzofuran-2-yl methyl ketone 1701-73-1, 1-(4-Pyridyl)pentan-1-one 5900-58-3, Methyl 2-amino-4-chlorobenzoate 6602-54-6, 2-Chloro-3-cyanopyridine 15871-85-9, 2-Methoxy-5-cyanopyridine 18781-31-2 22047-25-2, Acetylpyrazine 22720-75-8, 2-**Acetylbenzothiophene** 22971-32-0, 1-(2-Pyridyl)butan-1-one 26414-90-4 27443-36-3 33252-30-1, 2-Chloro-4-cyanopyridine 82736-91-2 88653-55-8, 2-Acetyl-5-**cyanothiophene** 349112-16-9
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)

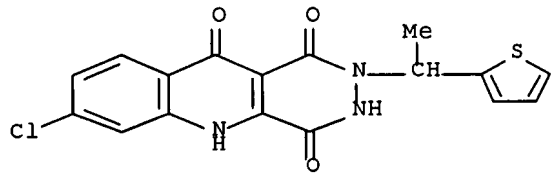
IT 1701-71-9P 3238-55-9P 6952-53-0P 106728-59-0P 109352-68-3P
109352-88-7P 109352-93-4P 109352-96-7P 113143-16-1P 170143-39-2P
182887-52-1P 182887-56-5P 349110-82-3P 349111-97-3P 349111-98-4P
349112-00-1P 349112-01-2P 349112-02-3P 349112-03-4P 349112-04-5P
349112-05-6P 349112-06-7P 349112-07-8P 349112-08-9P 349112-09-0P
349112-10-3P 349112-11-4P 349112-12-5P 349112-13-6P 349112-14-7P
349112-15-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)

RETABLE

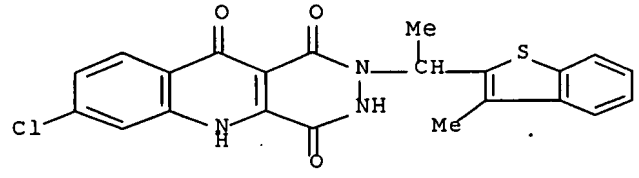
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Zeneca Limited	1995			WO 9511244 A1	HCAPLUS
Zeneca Limited	1996			EP 0736531 A1	HCAPLUS

IT **349111-92-8P 349111-93-9P 349111-94-0P**
349111-95-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1,2,5,10-**tetrahydropyridazino**[4,5-b]quinoline-1,10-diones for the treatment of pain)

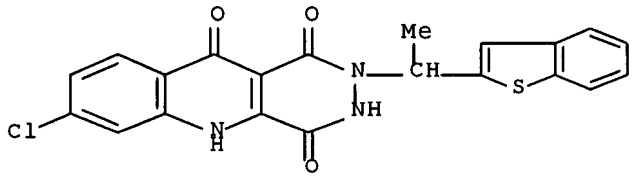
RN 349111-92-8 HCAPLUS
CN Pyridazino[4,5-b]quinoline-1,4,10(5H)-trione, 7-chloro-2,3-dihydro-2-[1-(2-thienyl)ethyl]- (9CI) (CA INDEX NAME)



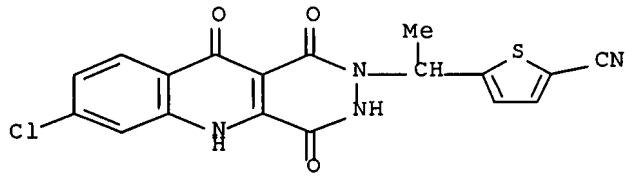
RN 349111-93-9 HCAPLUS
CN Pyridazino[4,5-b]quinoline-1,4,10(5H)-trione, 7-chloro-2,3-dihydro-2-[1-(3-methylbenzo[b]thien-2-yl)ethyl]- (9CI) (CA INDEX NAME)



RN 349111-94-0 HCAPLUS
CN Pyridazino[4,5-b]quinoline-1,4,10(5H)-trione, 2-(1-benzo[b]thien-2-ylethyl)-7-chloro-2,3-dihydro- (9CI) (CA INDEX NAME)



RN 349111-95-1 HCAPLUS
CN 2-Thiophenecarbonitrile, 5-[1-(7-chloro-3,4,5,10-tetrahydro-1,4,10-trioxopyridazino[4,5-b]quinolin-2(1H)-yl)ethyl]- (9CI) (CA INDEX NAME)



L99 ANSWER 16 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:416941 HCAPLUS Full-text
DOCUMENT NUMBER: 135:33489
TITLE: Pyrazolopyrazines and their use as adenosine antagonists
INVENTOR(S): Akahane, Atsushi; Kuroda, Satoru; Itani, Hiromichi; Tabuchi, Seiichiro; Sato, Yoshiniro; Matsuoka, Nobuya; Tada, Miho; Matsuoka, Hideaki; Oku, Takuma; Tanaka, Akira
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040230	A1	20010607	WO 2000-JP8008	20001113 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1244669	A1	20021002	EP 2000-974973	20001113 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2003515537 T 20030507 JP 2001-540985 20001113 <--
PRIORITY APPLN. INFO.: AU 1999-4414 A 19991202 <--
WO 2000-JP8008 W 20001113 <--
OTHER SOURCE(S): MARPAT 135:33489
ED Entered STN: 08 Jun 2001
AB A pyrazolopyrazine compound of formula I is claimed [wherein R1 = (un)substituted aryl; R2 = H, lower alkyl, lower alkenyl, cyclo(lower)alkyl, heteromonocyclic group, lower alkyl (un)substituted by one or more of cyclo(lower)alkyl, halogen, cyano, aryl and heteromonocyclic group; or a salt thereof]. I are adenosine antagonists, and are useful for the prevention and/or treatment of a wide variety of conditions known to be related to adenosine receptors, including depression, dementia (e.g., Alzheimer's disease, cerebrovascular dementia, dementia accompanying Parkinson's disease, etc.), Parkinson's disease, anxiety, pain, cerebrovascular disease (e.g. stroke, etc.), heart failure, and the like. Over 60 examples and various intermediates were prepared For instance, 6-benzenesulfonyl-2H-**pyridazin**-3-one was converted to its O-triflate, which was coupled with phenylacetylene and then cyclized with 1-aminopyrazinium iodide to give 3-(6-**benzenesulfonylpyridazin**** * -3-yl)-2-**phenylpyrazolo[1,5-a]pyrazine. The latter was hydrolyzed to remove the benzenesulfonyl group and then coupled with 3-pyridinemethanol by Mitsunobu reaction to give title compound II. Six selected I bound to A1 and A2a receptors with Ki ranges of 0.06-0.16 nM and 0.84-3.17 nM, resp. Four compds. also gave complete or near-complete reversal of haloperidol-induced catalepsy in mice at 3.2 mg/kg.
IC ICM C07D487-04
ICS A61K031-495; A61P025-28; A61P025-16; A61P025-22; A61P009-04; A61P001-04; A61P001-18; A61P013-12; A61P009-10
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
ST pyrazolopyrazine prepn adenosine antagonist; anticataleptic
***pyridazinyl** pyrazolopyrazine prepn
IT 343792-04-1P 343792-05-2P 343792-06-3P 343792-07-4P 343792-08-5P
343792-09-6P 343792-10-9P 343792-11-0P 343792-12-1P 343792-13-2P
343792-14-3P 343792-15-4P **343792-16-5P** 343792-17-6P
343792-18-7P 343792-19-8P 343792-20-1P 343792-21-2P 343792-22-3P
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343792-29-0P 343792-30-3P 343792-32-5P 343792-33-6P 343792-34-7P
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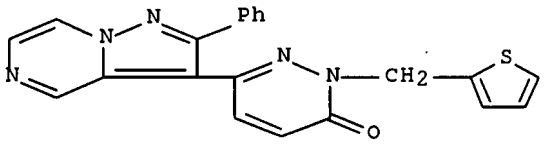
343792-43-8P 343792-44-9P 343792-45-0P 343792-46-1P 343792-47-2P
343792-48-3P 343792-49-4P 343792-50-7P 343792-51-8P 343792-52-9P
343792-54-1P 343792-55-2P 343792-56-3P 343792-58-5P 343792-59-6P
343792-60-9P 343792-61-0P 343792-62-1P 343792-63-2P 343792-64-3P
343792-65-4P 343792-66-5P 343792-67-6P 343792-68-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrazolopyrazines as adenosine antagonists)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Akahane	1998			US 5773530 A	HCAPLUS
Fujisawa	1990			EP 0379979 A	HCAPLUS
Fujisawa	1992			EP 0467248 A	HCAPLUS

IT **343792-16-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrazolopyrazines as adenosine antagonists)

RN 343792-16-5 HCAPLUS
CN 3(2H)-Pyridazinone, 6-(2-phenylpyrazolo[1,5-a]pyrazin-3-yl)-2-(2-thienylmethyl)- (9CI) (CA INDEX NAME)



L99 ANSWER 17 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:772163 HCAPLUS Full-text
DOCUMENT NUMBER: 135:318510
TITLE: Preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors
INVENTOR(S): Black, Lawrence A.; Basha, Anwer; Kolasa, Teodozyj; Kort, Michael E.; Liu, Huaqing; McCarty, Catherine M.; Patel, Meena; Rohde, Jeffrey J.; Coghlan, Michael J.; Stewart, Andrew O.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: U.S., 129 pp., Cont.-in-part of U.S. Ser. No. 261,872, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6307047	B1	20011023	US 1999-427768	19991027 <--
TR 200000478	T2	20020422	TR 2000-200000478	19980810 <--
CA 2347982	A1	20000504	CA 1999-2347982	19991027 <--
WO 2000024719	A1	20000504	WO 1999-US25234	19991027 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9965230	A1	20000515	AU 1999-65230	19991027 <--
AU 773237	B2	20040520		
EP 1124804	A1	20010822	EP 1999-953259	19991027 <--
EP 1124804	B1	20050824		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9914858	A	20020205	BR 1999-14858	19991027 <--
TR 200101765	T2	20020221	TR 2001-200101765	19991027 <--
HU 200105248	A2	20020729	HU 2001-5248	19991027 <--
JP 2003512292	T	20030402	JP 2000-578289	19991027 <--
AT 302759	T	20050915	AT 1999-953259	19991027 <--

ES 2249919	T3	20060401	ES 1999-953259		19991027 <--
ZA 2001003310	A	20020723	ZA 2001-3310		20010423 <--
NO 2001002061	A	20010627	NO 2001-2061		20010426 <--
NO 318623	B1	20050418			
BG 105523	A	20011231	BG 2001-105523		20010519 <--
US 2002013318	A1	20020131	US 2001-871195		20010531 <--
US 2002028938	A1	20020307	US 2001-870838		20010531 <--
HK 1041876	A1	20060623	HK 2002-101207		20020219 <--
US 2003225276	A1	20031204	US 2003-417959		20030417 <--
US 7001895	B2	20060221			
US 2004158064	A1	20040812	US 2003-464928		20030619 <--
US 7115591	B2	20061003			
PRIORITY APPLN. INFO.:			US 1997-56733P	P	19970822 <--
			US 1998-129570	B2	19980805 <--
			US 1998-137457	B2	19980820 <--
			US 1998-179605	B2	19981027 <--
			US 1999-261872	B2	19990303 <--
			US 1997-917023	A	19970822 <--
			US 1999-298490	A	19990423 <--
			US 1999-427768	A	19991027 <--
			WO 1999-US25234	W	19991027 <--
			US 2001-870838	B3	20010531 <--
			US 2001-871195	B3	20010531 <--

OTHER SOURCE(S): MARPAT 135:318510

ED Entered STN: 24 Oct 2001

AB The title compds. [I; X = O, S, NR4, etc.; R4 = alkyl, alkenyl, cycloalkyl, etc.; R = H, alkyl, alkenyl, etc.; at least one of R1-R3 = II-III (wherein X1 = SO2, SO(NR10), SO, etc.; R9 = alkyl, alkenyl, alkynyl, etc.; X2 = H, halo, alkyl, etc.; R10 = H, alkyl, cycloalkyl); the remaining two of the groups of R1-R3 = H, OH, hydroxyalkyl, etc.] which are cyclooxygenase (COX) inhibitors, and in particular, are selective inhibitors of cyclooxygenase-2 (COX-2), and therefore are useful in treating pain, fever, inflammation, rheumatoid arthritis, and osteoarthritis, were prepared Thus, oxidation of 2-benzyl-4-(4-fluorophenyl)-5- [4-(methylthio)phenyl]-3(2H)-**pyridazinone** (preparation given) with MeCO3H in CH2Cl2 afforded 86% I [X = O; R = PhCH2; R1 = 4-FC6H4; R2 = 4-(MeSO2)C6H4; R3 = H], which showed IC50 of 0.014 μM against COX-2. COX-2 is the inducible isoform associated with inflammation, as opposed to the constitutive isoform, cyclooxygenase-1 (COX-1) which is an important "housekeeping" enzyme in many tissues, including the gastrointestinal (GI) tract and the kidneys. The selectivity of the compds. I for COX-2 minimizes the unwanted GI and renal side-effects seen with currently marketed non-steroidal anti-inflammatory drugs (NSAIDs).

IC ICM C07D237-16
ICS C07F009-6509; A61K031-50; A61K031-675

INCL 544240000

CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST prostaglandin endoperoxide H synthase biosynthesis inhibitor **arylpyridazinone** prepn; **arylpyridazinone** prepn prostaglandin endoperoxide H synthase biosynthesis inhibitor; cyclooxygenase 2 selective inhibitor **arylpyridazinone** prepn; analgesic **arylpyridazinone** prepn; antipyretic **arylpyridazinone** prepn; antiinflammatory **arylpyridazinone** prepn; rheumatoid arthritis **arylpyridazinone** prepn; osteoarthritis **arylpyridazinone** prepn; antiarthritic **arylpyridazinone** prepn

IT Analgesics
Anti-inflammatory agents
Antiarthritics
Antipyretics

(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT Osteoarthritis
(treatment of; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 655-20-9P 2514-18-3P 14092-00-3P 28075-50-5P 34837-84-8P
40400-25-7P 51437-00-4P, 1-Bromo-4-fluoro-3-methylbenzene 59982-04-6P
63031-77-6P 84956-71-8P 89981-03-3P 97137-16-1P 98546-51-1P
109715-47-1P 134965-39-2P 161886-22-2P, 3,4-Difluorophenylhydrazine
213764-19-3P 221025-49-6P 221025-50-9P 221025-51-0P 221030-72-4P
221030-73-5P 221030-74-6P 221030-75-7P 221030-76-8P 221030-77-9P
221030-78-0P 221030-79-1P 221030-80-4P 221030-81-5P 221030-82-6P
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221031-38-5P 221031-39-6P 221031-40-9P 221031-41-0P 266320-87-0P
266320-88-1P 266320-89-2P 266320-90-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 39391-18-9, Prostaglandin endoperoxide H synthase
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 109715-46-0 266320-84-7 266320-85-8 266320-86-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 221031-64-7P 221031-65-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 62-53-3, Benzenamine, reactions 65-85-0, Benzoic acid, reactions 67-63-0, 2-Propanol, reactions 70-11-1, 2-Bromoacetophenone 71-36-3, n-Butanol, reactions 75-31-0, 2-Aminopropane, reactions 75-33-2, Isopropyl mercaptan 75-65-0, Tert-Butanol, reactions 75-66-1, 2-Methyl-2-propanethiol 75-84-3 78-83-1, Reactions, reactions 87-56-9, Mucochloric acid 92-66-0, 4-Bromobiphenyl 92-69-3, 4-Phenylphenol 96-41-3, Cyclopentanol 97-95-0, 2-Ethyl-1-butanol 98-00-0, 2-(Hydroxymethyl)furan 98-02-2, Furfuryl mercaptan 98-59-9, p-Toluenesulfonyl chloride 99-07-0, 3-(Dimethylamino)phenol 100-11-8 100-39-0 100-44-7, reactions 100-51-6, Benzyl alcohol, reactions 100-53-8, Benzyl mercaptan 101-55-3, 4-Bromodiphenylether 102-56-7, 2,5-Dimethoxyaniline 103-63-9, (2-Bromoethyl)benzene 103-67-3, N-Methylbenzylamine 103-90-2 104-76-7 104-95-0, 4-Bromothioanisole 106-37-6, 1,4-Dibromobenzene 106-38-7, 1-Bromo-4-methylbenzene 106-39-8, 4-Bromo-1-chlorobenzene 106-41-2, p-Bromophenol 106-48-9, p-Chlorophenol 106-96-7, Propargyl bromide 107-18-6, 2-Propen-1-ol, reactions 107-82-4, 1-Bromo-3-methylbutane 108-01-0 108-11-2, 4-Methyl-2-pentanol 108-36-1, 1,3-Dibromobenzene 108-37-2,

1-Bromo-3-chlorobenzene 108-85-0, Cyclohexyl bromide 108-91-8, Cyclohexanamine, reactions 108-93-0, Cyclohexanol, reactions 108-94-1, Cyclohexanone, reactions 108-95-2, Phenol, reactions 109-00-2, 3-Hydroxypyridine 109-59-1, 2-(Isopropoxy)ethanol 110-63-4, 1,4-Butanediol, reactions 110-87-2 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 116-09-6, Acetol 120-20-7, 3,4-Dimethoxyphenethylamine 123-51-3 123-75-1, Pyrrolidine, reactions 126-30-7 137-43-9, Cyclopentyl bromide 150-76-5, 4-Methoxyphenol 151-18-8 156-87-6, 3-Hydroxypropylamine 339-62-8 348-57-2, 2,4-Difluorobromobenzene 348-61-8, 1-Bromo-3,4-difluorobenzene 349-55-3, 3-Methoxy-5-(trifluoromethyl)aniline 352-13-6, 4-Fluorophenylmagnesium bromide 352-34-1, 4-Fluoroiodobenzene 353-83-3, 2-Iodo-1,1,1-trifluoroethane 363-80-4, 2,3,5-Trifluoroaniline 367-11-3, 1,2-Difluorobenzene 367-25-9, 2,4-Difluoroaniline 367-67-9, 2-Bromo-5-nitrobenzotrifluoride 368-78-5, 3-(Trifluoromethyl)phenylhydrazine 371-14-2 371-40-4, 4-Fluoroaniline 371-41-5, 4-Fluorophenol 372-19-0, 3-Fluoroaniline 372-20-3, 3-Fluorophenol 383-53-9, 2-Bromo-4'-(trifluoromethyl)acetophenone 395-44-8, 2-(Trifluoromethyl)benzyl bromide 401-81-0 402-43-7, 1-Bromo-4-trifluoromethylbenzene 403-41-8, 4-Fluoro-α-methylbenzyl alcohol 405-50-5, 4-Fluorophenylacetic acid 456-41-7, 3-Fluorobenzyl bromide 459-46-1, 4-Fluorobenzyl bromide 460-25-3, 1,3-Dibromo-1,1-difluoropropane 461-96-1, 3,5-Difluorobromobenzene 488-11-9, Mucobromic acid 513-44-0, 2-Methyl-1-propanethiol 536-38-9, 2-Bromo-4'-chloroacetophenone 541-73-1 556-96-7, 5-Bromo-m-xylene 558-43-0, 2-Methyl-1,2-propanediol 563-47-3, 3-Chloro-2-methylpropene 577-19-5, 1-Bromo-2-nitrobenzene 589-35-5 590-90-9, 4-Hydroxy-2-butanone 591-17-3, 3-Bromotoluene 600-36-2, 2,4-Dimethyl-3-pentanol 619-57-8, 4-Hydroxybenzamide 622-26-4, 4-(2-Hydroxyethyl)piperidine 622-40-2, 4-(2-Hydroxyethyl)morpholine 623-00-7, 4-Bromobenzonitrile 624-95-3, 3,3-Dimethyl-1-butanol 626-88-0, 1-Bromo-4-methylpentane 626-89-1, 4-Methyl-1-pentanol 627-59-8, 5-Methyl-2-hexanol 636-98-6, 1-Iodo-4-nitrobenzene 645-56-7, 4-(n-Propyl)phenol 661-69-8, Hexamethylditin 700-57-2, 2-Adamantanol 701-34-8, 4-Aminosulfonyl-1-bromobenzene 763-32-6 763-89-3 765-58-2, 2-Bromo-5-**methylthiophene** 766-00-7, Cyclopentaneethanol 766-02-9, 2-Cyclopentene-1-ethanol 767-00-0, 4-Cyanophenol 823-85-8, 4-Fluorophenylhydrazine hydrochloride 870-63-3 873-74-5, 4-Aminobenzonitrile 924-41-4, 1,5-Hexadien-3-ol 931-51-1, Cyclohexylmagnesium chloride 1003-03-8, Cyclopentylamine 1003-09-4, 2-**Bromothiophene** 1072-85-1, 2-Fluorobromobenzene 1073-62-7, Benzylhydrazine hydrochloride 1121-86-4, 1-Fluoro-3-iodobenzene 1126-81-4, 4-**Acetamidothiophenol** 1423-26-3 1462-03-9, 1-Methyl-1-cyclopentanol 1521-51-3, 3-Bromocyclohexene 1544-53-2 1569-69-3, Cyclohexyl mercaptan 1643-73-8, 4-Fluorobenzylmagnesium chloride 1679-07-8, Cyclopentyl mercaptan 1679-18-1, 4-Chlorobenzeneboronic acid 1698-53-9, 2-Phenyl-4,5-dichloro-3(2H)-**pyridazinone** 1765-40-8, 2,3,4,5,6-Pentafluorobenzyl bromide 1765-93-1, 4-Fluorobenzeneboronic acid 1794-48-5 1826-67-1, Vinylmagnesium bromide 1996-29-8, 1-Bromo-4-chloro-2-fluorobenzene 2039-86-3, 3-Bromostyrene 2076-88-2, 2-(Chloromethyl)benzo[b]**thiophene** 2081-44-9, 4-Tetrahydropyranol 2113-57-7, 3-Bromobiphenyl 2156-04-9 2259-30-5, Tert-Butylmagnesium bromide 2312-23-4, 3-Chlorophenylhydrazine hydrochloride 2357-52-0, 3-Fluoro-4-methoxybromobenzene 2417-72-3, Methyl 4-(bromomethyl)benzoate 2516-33-8, Cyclopropylmethanol 2516-34-9, Cyclobutanamine 2516-47-4, Cyclopropanemethanamine 2517-43-3 2557-78-0, 2-**Fluorothiophenol** 2566-44-1, 2-(Cyclopropyl)ethanol 2567-14-8, 1,1,3-Trichloropropene 2568-33-4 2637-34-5, 2-Mercaptopyridine 2746-14-7, 1-Methylcyclopropanemethanol 2746-23-8, 3-(Chloromethyl)

thiophene 2799-16-8 2873-18-9, 2-Bromo-5-chlorothiophene 2924-16-5, 3-Fluorophenylhydrazine hydrochloride 2938-98-9, 2-Methyl-1,4-butanediol 3179-31-5, 1H-1,2,4-Triazole-3-thiol 3446-89-7, 4-Methylthiobenzaldehyde 3863-11-4 3958-57-4, 3-Nitrobenzyl bromide 3972-65-4, 1-Bromo-4-tert-butylbenzene 4254-29-9, 2-Indanol 4294-57-9, p-Tolylmagnesium bromide 4377-41-7, 2-(Chloromethyl)quinoline 4392-24-9, Cinnamyl bromide 4399-47-7, Cyclobutyl bromide 4548-78-1, 3-Methylbutylmagnesium bromide 4795-29-3, Tetrahydrofurfurylamine 5036-48-6, 1H-Imidazole-1-propanamine 5042-30-8, Trifluoroethylhydrazine 5271-38-5, 2-(Methylthio)ethanol 5332-73-0, 3-Methoxypropylamine 5362-55-0 5469-26-1, 1-Bromopinacolone 5673-98-3 5674-02-2, Isobutylmagnesium chloride 5713-61-1, 2-Thienylmagnesium bromide 5720-05-8, 4-Methylphenylboronic acid 5720-06-9, 2-Methoxybenzeneboronic acid 5788-58-9, 4,5-Dibromo-3(2H)-pyridazinone 6165-69-1, Thiophene-3-boronic acid 6351-10-6, 1-Indanol 6630-33-7, 2-Bromobenzaldehyde 6738-06-3, Phenylacetylenemagnesium bromide 6921-34-2, Benzylmagnesium chloride 7051-34-5 7342-82-7, 3-Bromobenzothiophene 7400-27-3, Tert-Butylhydrazine hydrochloride 7417-21-2, 2-(3,4-Dimethoxyphenyl)ethanol 7429-94-9 10493-44-4 13124-18-0, 3,4-Dichlorophenylhydrazine 13195-50-1, 2-Bromo-5-nitrothiophene 13291-18-4, Isopropenylmagnesium bromide 13331-27-6, 3-Nitrobenzeneboronic acid 14114-05-7, Cyclopropyltriphenylphosphonium bromide 14282-76-9, 2-Bromo-3-methylthiophene 14300-71-1 14763-20-3 14763-60-1, 4-(Methylsulfonyl)phenol 14916-80-4, 3-Octyn-1-ol 15894-04-9 16419-60-6 16466-97-0 18729-48-1, 3-Methylcyclopentanol 19477-73-7, 6-Bromophthalide 19614-16-5, 2-Bromothioanisole 20099-89-2, 2-Bromo-4'-cyanoacetophenone 22037-28-1, 3-Bromofuran 22884-29-3, Isobutyltriphenylphosphonium bromide 23915-07-3, 2,4-Difluorobenzyl bromide 24070-77-7, 2-Methylcyclopentanol 26167-44-2, 3-Chloroacetylbenzo[b]thiophene 26445-03-4, Thiocresol 27246-81-7, 3-Bromophenylhydrazine hydrochloride 27314-17-6 28322-40-9, Isoamyltriphenylphosphonium bromide 32916-51-1, Cyclopentylmagnesium chloride 33577-16-1, Methyl(methylsulfinylmethyl)sulfide 33598-19-5 33733-73-2, 3-Bromothioanisole 33884-43-4, 2-(2-Bromoethyl)-1,3-dioxane 34698-41-4, 1-Indanylamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of arylpyridazinones as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 35166-78-0, Cyclohexylmethylmagnesium bromide 37677-17-1, 1-Bromomethylcyclohexene 39720-27-9, 4-(Chloromethyl)phenyl acetate 40594-37-4, 3,4-Difluorophenylhydrazine hydrochloride 40811-49-2, 2-(Isopropylthio)ethanol 50398-79-3, 2-(Bromomethyl)-5-chlorothiazole 51336-94-8, 2-Chloro-2',4'-difluoroacetophenone 51755-66-9, 3-(Methylthio)-1-hexanol 52497-07-1, 1,3-Dichloro-1-butene 54751-01-8, 4-(Bromomethyl)pyridine 55401-97-3, 2-(Bromomethyl)pyridine 55499-43-9 55766-17-1 56816-01-4, Ethyl (S)-3-hydroxybutanoate 58114-09-3 59311-22-7 59311-24-9 60811-18-9, 4-Bromo-1-chloro-2-fluorobenzene 60811-21-4 60811-23-6, 3-Chloro-4-fluorothiophenol 62087-82-5, 1-Adamantyl fluoroformate 64168-34-9, 3-Fluorobenzylmagnesium chloride 65130-46-3 69966-55-8, 3-(Bromomethyl)pyridine 72396-61-3 72657-23-9 80657-57-4, Methyl (S)-3-hydroxy-2-methylpropionate 82297-89-0, 4-Fluoro-3-methylphenylmagnesium bromide 84282-78-0 85118-01-0, 3,4-Difluorobenzyl bromide 85676-85-3 90555-66-1 90878-19-6, Phenethylmagnesium chloride 92636-36-7 93777-26-5, 5-Bromo-2-fluorobenzaldehyde 98437-24-2, 2-Benzofuranboronic acid 103962-10-3, 2-Bromo-4'-(trifluoromethoxy)acetophenone 112615-82-4, 5-Methylhexylmagnesium bromide 122957-82-8 124050-15-3, 2-(Chloromethyl)-6-fluoroquinoline 128758-41-8 128796-39-4,

4-(Trifluoromethyl)benzeneboronic acid 134150-01-9 137504-86-0, 3-Fluoro-4-chlorophenylboronic acid 141483-15-0, 2-Fluoro-5-trifluoromethylphenol 144432-85-9, 3-Chloro-4-fluorobenzeneboronic acid 149507-26-6 151411-98-2 157911-55-2 157911-56-3 162125-08-8, 3,4-Dichlorophenylboronic acid 162607-18-3 163105-90-6 168267-99-0 171497-20-4 172975-69-8 175135-73-6 175135-74-7 208641-98-9 221020-96-8 221031-42-1 221031-43-2 221031-44-3 221031-45-4 221031-46-5 221031-47-6 221031-48-7 221031-49-8 221031-50-1 221031-51-2 221031-52-3 221031-53-4 221031-54-5 221031-55-6 221031-56-7 221031-57-8 221031-58-9 221031-59-0 221031-60-3 221031-61-4 221031-62-5 221031-63-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 213763-90-7P 213764-00-2P 213764-17-1P 221025-44-1P 221025-45-2P
221025-46-3P 221025-47-4P 221025-52-1P 221025-53-2P 221025-77-0P
221026-16-0P 221026-30-8P 221026-34-2P 221026-35-3P 221026-45-5P
221026-46-6P 221026-51-3P 221026-61-5P 221026-62-6P 221026-78-4P
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221029-47-6P 221029-50-1P 221029-69-2P 221029-78-3P 221029-80-7P
221029-81-8P 221029-83-0P 221029-84-1P 221029-86-3P 221030-47-3P
221030-56-4P 221030-64-4P 221030-66-6P 221030-67-7P 266320-83-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 213763-92-9P 213763-94-1P 213763-98-5P 213763-99-6P 213764-11-5P
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221025-73-6P **221025-74-7P** 221025-75-8P 221025-76-9P
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221028-62-2P 221028-63-3P 221028-64-4P 221028-65-5P 221028-66-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

IT 221028-67-7P 221028-68-8P 221028-69-9P 221028-70-2P 221028-71-3P
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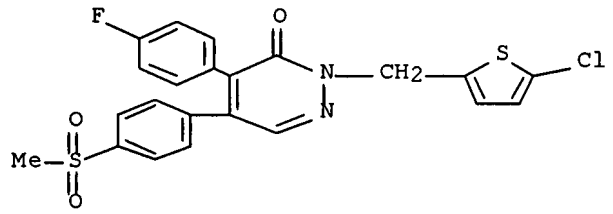
266320-17-6P 266320-18-7P 266320-19-8P 266320-20-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

RETABLE

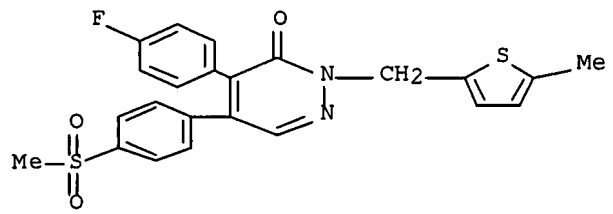
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Anon	1988			WO 8809675	HCAPLUS
Anon	1996			EP 0711759	HCAPLUS
Anon	1996			EP 0714895	HCAPLUS
Anon	1999			WO 9910331	HCAPLUS
Griswold	1986	16	181	Medicinal Research R	
Li	1999			US 6004960	HCAPLUS
Sircar	1983			US 4404203	HCAPLUS
Vane	1994	367	215	Nature	MEDLINE

IT **221025-73-6P 221025-74-7P 221025-98-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of **arylpyridazinones** as prostaglandin endoperoxide H synthase biosynthesis inhibitors)

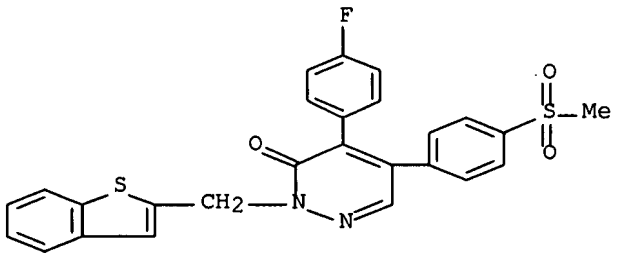
RN 221025-73-6 HCAPLUS
CN 3(2H)-Pyridazinone, 2-[(5-chloro-2-thienyl)methyl]-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



RN 221025-74-7 HCAPLUS
CN 3(2H)-Pyridazinone, 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-2-[(5-methyl-2-thienyl)methyl]- (9CI) (CA INDEX NAME)



RN 221025-98-5 HCAPLUS
CN 3(2H)-Pyridazinone, 2-(benzo[b]thien-2-ylmethyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



L99 ANSWER 18 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:635750 HCAPLUS Full-text
DOCUMENT NUMBER: 129:275920
TITLE: Preparation of **pyridazinones** as inhibitors of cyclooxygenase-2
INVENTOR(S): Li, Chun Sing; Prasit, Petpiboon; Gauthier, Jacques Y.; Lau, Cheuk K.; Therien, Michel
PATENT ASSIGNEE(S): Merck Frosst Canada Inc., Can.
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9841511	A1	19980924	WO 1998-CA233		19980312	<--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU						
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG						
CA 2283399	A1	19980924	CA 1998-2283399		19980312	<--
CA 2283399	C	20060221				
AU 9864913	A	19981012	AU 1998-64913		19980312	<--
AU 738727	B2	20010927				
EP 975604	A1	20000202	EP 1998-910544		19980312	<--
EP 975604	B1	20040721				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI						
JP 2001514669	T	20010911	JP 1998-539982		19980312	<--
AT 271547	T	20040815	AT 1998-910544		19980312	<--
ES 2224366	T3	20050301	ES 1998-910544		19980312	<--
US 6004960	A	19991221	US 1998-42174		19980313	<--
PRIORITY APPLN. INFO.:			US 1997-40791P	P	19970314	<--
			GB 1997-7487	A	19970414	<--
			WO 1998-CA233	W	19980312	<--

OTHER SOURCE(S): MARPAT 129:275920
ED Entered STN: 08 Oct 1998

AB The title compds. [I; X = a bond, (CH2)m (m = 1-2); CO, etc.; R1 = Me, NH2. NHC(O)CF3; R2 = (CR6R7)nR8 (R6, R7 = H, C1-10 alkyl, C1-10 fluoroalkyl; R8 = C1-10 alkyl, (un)substituted Ph, naphthyl, etc.); R3 = C1-10 alkyl, (un)substituted Ph, naphthyl, etc.; R4 = H, halo, C1-6 alkyl], useful in treating an inflammatory disease susceptible to treatment with a non-steroidal antiinflammatory agent, and cyclooxygenase-2 mediated diseases, were prepared Thus, reaction of 5-hydroxy-4-(4-methylsulfonyl)phenyl-3-phenyl-5H-furan-2-one with phenylhydrazine in EtOH afforded 30% I [X = a bond; R1 = Me; R2 = Ph; R3 = Ph; R4 = H] which showed IC50 of 0.08 against COX-2 using CHO cell line assay.

IC ICM C07D237-04
ICS A61K031-50

CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST **pyridazinone** prepn cyclooxygenase selective inhibitor; antiinflammatory **pyridazinone** prepn

IT Anti-inflammatory agents
(treating an inflammatory disease susceptible to treatment with a non-steroidal antiinflammatory agent; preparation of **pyridazinones** as inhibitors of cyclooxygenase-2)

IT 39391-18-9
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(2; selective COX-2 inhibitor; preparation of **pyridazinones** as inhibitors of cyclooxygenase-2)

IT 213763-79-2P 213763-80-5P 213763-81-6P 213763-82-7P 213763-83-8P
213763-84-9P 213763-85-0P 213763-86-1P 213763-87-2P 213763-88-3P
213763-89-4P 213763-90-7P 213763-91-8P 213763-92-9P 213763-93-0P
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213764-13-7P 213764-14-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **pyridazinones** as inhibitors of cyclooxygenase-2)

IT 67-63-0, Isopropanol, reactions 75-30-9, 2-Iodopropane 96-32-2, Methyl bromoacetate 100-39-0, Benzyl bromide 100-63-0, Phenylhydrazine 345-35-7, 2-Fluorobenzyl chloride 371-41-5, 4-Fluorophenol 456-42-8, 3-Fluorobenzyl chloride 459-46-1, 4-Fluorobenzyl bromide 460-37-7, 3,3,3-Trifluoropropyl iodide 461-17-6, 4,4,4-Trifluorobutyl iodide 488-11-9, Mucobromic acid 513-38-2, 2-Methylpropyl iodide 585-71-7, (1-Bromoethyl)benzene 626-55-1, 3-Bromopyridine 630-17-1, 2,2-Dimethylpropyl bromide 1822-51-1, 4-Chloromethylpyridine hydrochloride 2417-72-3, 4-Carbomethoxybenzyl bromide 2550-36-9, Bromomethylcyclohexane 2924-16-5, 3-Fluorophenylhydrazine hydrochloride 3510-66-5, 2-Bromo-5-methylpyridine 4214-79-3, 5-Chloro-2-pyridinol 5042-30-8, 2,2,2-Trifluoroethylhydrazine 5419-55-6 5788-58-9 6959-47-3, 2-Picolyl chloride hydrochloride 7051-34-5, (Bromomethyl)cyclopropane 17247-58-4, Bromomethylcyclobutane 20570-96-1, Benzylhydrazine dihydrochloride 45438-73-1, 2-(Bromomethyl) **thiophene** 98546-51-1, 4-(Methylthio)phenylboronic acid 185147-17-5 185147-18-6 189956-44-3 213764-23-9 213764-24-0 213764-25-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **pyridazinones** as inhibitors of cyclooxygenase-2)

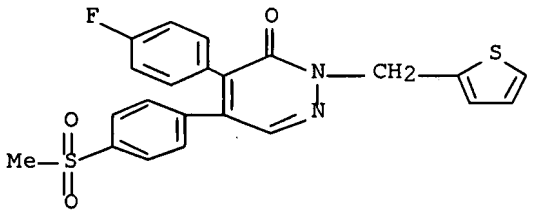
IT 134965-39-2P 213764-15-9P 213764-16-0P 213764-17-1P 213764-18-2P
213764-19-3P 213764-20-6P 213764-21-7P 213764-22-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation of **pyridazinones** as inhibitors of cyclooxygenase-2)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Diamond Shamrock Corp	1983			WO 8300863 A	HCAPLUS
Merck Frosst Canada Inc	1995			WO 9518799 A	HCAPLUS
Merck Frosst Canada Inc	1996			WO 9606840 A	HCAPLUS
Nissan Chemical Ind Ltd	1990			EP 0376079 A	HCAPLUS
Partis, R	1996			WO 9624584 A	HCAPLUS
Searle & Co	1996			WO 9641626 A	HCAPLUS
Searle & Co	1996			WO 9641645 A	HCAPLUS
Yves, G	1995			WO 9500501 A	HCAPLUS
Yves, G	1998			WO 9803484 A	HCAPLUS

IT **213764-05-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **pyridazinones** as inhibitors of cyclooxygenase-2)
RN 213764-05-7 HCAPLUS
CN 3(2H)-Pyridazinone, 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-2-(2-thienylmethyl)- (9CI) (CA INDEX NAME)



L99 ANSWER 19 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:186492 HCAPLUS Full-text
DOCUMENT NUMBER: 128:230388
TITLE: Preparation of 4-aminopyrimidines for control of diabetic complications.
INVENTOR(S): Mylari, Banavara L.; Oates, Peter J.; Siegel, Todd W.; Zembrowski, William J.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 30 pp., Cont.-in-part of U.S. Ser. No. 952,222, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5728704	A	19980317	US 1995-406947	19950324 <--
WO 9407867	A1	19940414	WO 1993-US6446	19930712 <--

W: AU, CA, JP, KR, NO, NZ, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

IL 121837	A	20030312	IL 1993-121837	19930923 <--
US 5866578	A	19990202	US 1997-980559	19971201 <--
PRIORITY APPLN. INFO.:			US 1992-952222	B2 19920928 <--
			WO 1993-US6446	W 19930712 <--
			IL 1993-107085	A3 19930923 <--
			US 1995-406947	A1 19950324 <--

OTHER SOURCE(S): MARPAT 128:230388

ED Entered STN: 30 Mar 1998

AB Title compds. [I; R1 = H, CF3, alkyl, alkylthioalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, hydroxyalkyl, alkoxy, Ph, naphthyl, etc.; R2, R3 = H, alkyl, (substituted) Ph, phenylalkyl; R2R3N = (substituted) azetidino, pyrrolidino, piperidino, piperazino, morpholino; R4 = H, Cl, Br, cyano, NO2, CF3, amino, alkyl, hydroxyalkyl, alkoxy, (substituted) Ph, naphthyl, furyl; R5 = H, alkyl, alkoxy, CF3, hydroxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, (substituted) Ph, furyl], were prepared Thus, 4-[4-(N-methylsulfamoyl)piperazino]-2-hydroxymethylpyrimdine (bioprepn. given) inhibited sorbitol dehydrogenase with IC50 = 1 μM.

IC ICM A71K031-505
ICS C07D401-04

INCL 514256000

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT **204456-53-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-aminopyrimidines for control of diabetic complications)

IT 131816-54-1 140687-51-0 **204456-54-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 4-aminopyrimidines for control of diabetic complications)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Albeck	1992			US 5102908	HCAPLUS
Anon	1954			FR 1063014	
Anon	1964			GB 0959699	
Anon	1982			EP 0047190	
Anon	1982			EP 0055693	HCAPLUS
Anon	1987			EP 0218999	HCAPLUS
Anon	1990			EP 0384370	HCAPLUS
Anon	1992			EP 0470616	HCAPLUS
Anon	1992			EP 9204333	
Brittain	1981			US 4251528	HCAPLUS
Brittain	1992			US 5110808	HCAPLUS
Brown	1992			US 5102905	HCAPLUS
Eggler	1991			US 5039672	HCAPLUS
Geisen	1992			US 5138058	HCAPLUS
Larson	1990			US 4939140	HCAPLUS
Lipinski	1989			US 4835410	
Lipinski	1991			US 5066659	HCAPLUS
Mallion	1992			US 5096918	HCAPLUS
Mattson	1992			US 5098904	HCAPLUS
Mylari	1991			US 4996204	HCAPLUS
Mylari	1991	34	109	Journal of Medicinal	
Mylari	1992	35	2155	Journal of Medicinal	HCAPLUS
Mylari	1992	35	457	Journal of Medicinal	HCAPLUS
Sarges	1978			US 4130714	HCAPLUS
Sestanj	1984			US 4439617	HCAPLUS
Yanagisawa	1988			US 4734410	HCAPLUS

York |1989 | | |US 4864028 |HCAPLUS

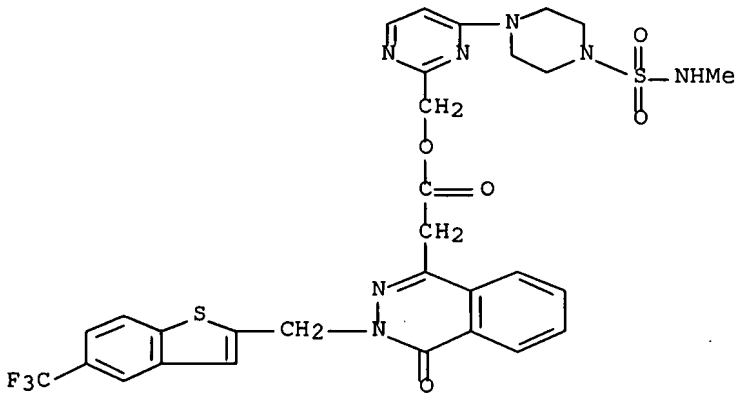
IT **204456-53-1P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 4-aminopyrimidines for control of diabetic complications)

RN 204456-53-1 HCAPLUS

CN 1-Phthalazineacetic acid, 3,4-dihydro-4-oxo-3-[[5-(trifluoromethyl)benzo[b]thien-2-yl]methyl]-, [4-[4-[(methylamino)sulfonyl]-1-piperazinyl]-2-pyrimidinyl]methyl ester (9CI) (CA INDEX NAME)



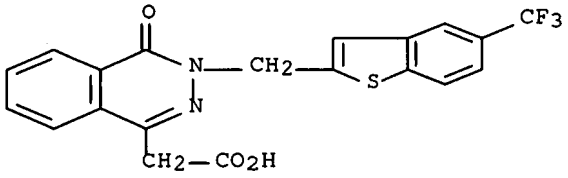
IT **204456-54-2**

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of 4-aminopyrimidines for control of diabetic complications)

RN 204456-54-2 HCAPLUS

CN 1-Phthalazineacetic acid, 3,4-dihydro-4-oxo-3-[[5-(trifluoromethyl)benzo[b]thien-2-yl]methyl]- (9CI) (CA INDEX NAME)



L99 ANSWER 20 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:719673 HCAPLUS Full-text

DOCUMENT NUMBER: 128:13276

TITLE: 1-(Arylsulfonyl)-, 1-(arylcarbonyl)-, and 1-(arylphosphonyl)-3-phenyl-1,4,5,6-**tetrahydropyridazines**

INVENTOR(S): Combs, Donald W.

PATENT ASSIGNEE(S): Ortho Pharmaceutical Corp., USA

SOURCE: U.S., 28 pp., Cont.-in-part of U.S. Ser. No. 80,986, abandoned.

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5684151	A	19971104	US 1995-362476	19950306 <--
WO 9401412	A1	19940120	WO 1993-US6394	19930701 <--

W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SE, SK, UA
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, BG, CI, CM, GA, GN

PRIORITY APPLN. INFO.:	US 1992-906984	B1	19920701 <--
	US 1993-80986	B2	19930621 <--
	WO 1993-US6394	W	19930701 <--

ED Entered STN: 14 Nov 1997

AB Title compds. such as I [R = 2-naphthyl, (un)substituted Ph, 2-thienyl; R1 = H, Me; W = a bond, CH:CH; R2 = (un)substituted Ph, 2-naphthyl] were prepared Progestin receptor binding, progestational and antiprogestational activity, osteoblast cell proliferation, and CNS receptor binding of the products were determined

IC ICM C07D237-04
ICS C07D409-04; C07D237-26

INCL 544224000

CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST **pyridazine** arylsulfonyl arylcarbonyl arylphosphonyl prepn bioactivity; progestin agonist **tetrahydropyridazine** derivs; bone growth activity **tetrahydropyridazine** derivs; CNS receptor binding **tetrahydropyridazine** derivs; receptor progestin CNS binding **tetrahydropyridazine** derivs

IT Progesterone receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(1-(arylsulfonyl)-, 1-(arylcarbonyl)-, and 1-(arylphosphonyl)-3-phenyl-1,4,5,6-**tetrahydropyridazine** binding to)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(CNS; 1-(arylsulfonyl)-, 1-(arylcarbonyl)-, and 1-(arylphosphonyl)-3-phenyl-1,4,5,6-**tetrahydropyridazine** binding to)

IT Nervous system
(central, receptors; 1-(arylsulfonyl)-, 1-(arylcarbonyl)-, and 1-(arylphosphonyl)-3-phenyl-1,4,5,6-**tetrahydropyridazine** binding to CNS receptors)

IT Osteoblast
(growth; 1-(arylsulfonyl)-, 1-(arylcarbonyl)-, and 1-(arylphosphonyl)-3-phenyl-1,4,5,6-**tetrahydropyridazine** effects on)

IT 159798-97-7P 159798-98-8P 159799-02-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(1-(arylsulfonyl)-, 1-(arylcarbonyl)-, and 1-(arylphosphonyl)-3-phenyl-1,4,5,6-**tetrahydropyridazines** as progestin agonists)

IT 71094-17-2P 109809-47-4P 159797-68-9P 159797-69-0P 159797-70-3P
159797-71-4P 159797-72-5P 159797-73-6P 159797-74-7P 159797-75-8P
159797-76-9P 159797-77-0P 159797-78-1P 159797-79-2P 159797-80-5P
159797-81-6P 159797-82-7P 159797-83-8P 159797-84-9P 159797-85-0P

159797-86-1P 159797-87-2P 159797-88-3P 159797-89-4P 159797-90-7P
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(1-(arylsulfonyl)-, 1-(arylcarbonyl)-, and 1-(arylphosphonyl)-3-phenyl-1,4,5,6-**tetrahydropyridazines** as progestin agonists)

IT 159800-08-5P 159800-09-6P 159800-10-9P 159800-11-0P 159800-12-1P
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159800-18-7P 159800-19-8P 159800-20-1P **159800-21-2P**
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159800-27-8P 159800-28-9P 159800-29-0P 159800-30-3P 159800-31-4P
159800-32-5P 159800-33-6P 159800-34-7P 159800-35-8P 199166-16-0P
199166-17-1P 199166-18-2P 199166-19-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(1-(arylsulfonyl)-, 1-(arylcarbonyl)-, and 1-(arylphosphonyl)-3-phenyl-1,4,5,6-**tetrahydropyridazines** as progestin agonists)

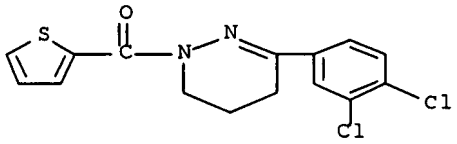
IT 77-73-6 95-13-6, Indene 98-60-2, Benzenesulfonyl chloride, 4-chloro- 98-61-3, Benzenesulfonyl chloride, 4-iodo- 378-77-8, Propanoic acid, pentafluoro-, sodium salt 527-69-5, 2-Furoyl chloride 532-27-4, 2-Chloroacetophenone 536-38-9, 2-Bromo-4'-chloroacetophenone 542-92-7, 1,3-Cyclopentadiene, reactions 672-75-3, Benzoyl chloride, 3-bromo-4-fluoro- 824-72-6, Phenylphosphonic dichloride 832-53-1, Benzenesulfonyl chloride, pentafluoro- 931-57-7, 1-Methoxycyclohexene 1314-80-3, Phosphorus pentasulfide 1576-35-8, p-Toluenesulfonyl hydrazide 2751-27-1, Benzenesulfonic acid, 4-iodo-, hydrazide 3024-72-4, Benzoyl chloride, 3,4-dichloro- 3140-93-0, **Thiophene**, 2,3-dibromo- 3984-34-7 4083-64-1, Tosyl isocyanate 5271-67-0, 2-**Thiophenecarbonyl** chloride 6335-44-0 15988-11-1, 4-Phenylurazole 18523-22-3, 2,3'-Dibromoacetophenone 52240-00-3 159800-62-1 159800-73-4 199166-21-7 199166-22-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(1-(arylsulfonyl)-, 1-(arylcarbonyl)-, and 1-(arylphosphonyl)-3-phenyl-1,4,5,6-**tetrahydropyridazines** as progestin agonists)

IT 1011-46-7P 1017-06-7P 1079-73-8P 24734-44-9P 36725-34-5P 36725-37-8P 52239-89-1P 52239-91-5P 52239-99-3P 66548-93-4P 66549-42-6P 92148-77-1P 117278-79-2P 136912-43-1P 136912-45-3P 136912-47-5P 152342-93-3P 159800-46-1P 159800-47-2P 159800-64-3P 159800-67-6P 159800-68-7P 159800-72-3P 199166-20-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(1-(arylsulfonyl)-, 1-(arylcarbonyl)-, and 1-(arylphosphonyl)-3-phenyl-1,4,5,6-**tetrahydropyridazines** as progestin agonists)

IT 57-83-0, Progestin, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(agonists; 1-(Arylsulfonyl)-, 1-(arylcarbonyl)-, and 1-(arylphosphonyl)-3-phenyl-1,4,5,6-**tetrahydropyridazines**)

IT **159800-21-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(1-(arylsulfonyl)-, 1-(arylcarbonyl)-, and 1-(arylphosphonyl)-3-phenyl-1,4,5,6-**tetrahydropyridazines** as progestin agonists)

RN 159800-21-2 HCAPLUS
CN Pyridazine, 3-(3,4-dichlorophenyl)-1,4,5,6-tetrahydro-1-(2-thienylcarbonyl)- (9CI) (CA INDEX NAME)



L99 ANSWER 21 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:476806 HCAPLUS Full-text
DOCUMENT NUMBER: 125:142755
TITLE: **Pyridazinoquinoline** compounds
INVENTOR(S): Bare, Thomas Michael; Chapdelaine, Marc Jerome; Davenport, Timothy Wayne; Empfield, James Roy; Garcia-Davenport, Laura Enid; Jackson, Paul Francis; McKinney, Jeffrey Alan; McLaren, Charles David;

	Sparks, Richard Bruce
PATENT ASSIGNEE(S):	Zeneca Limited, UK
SOURCE:	PCT Int. Appl., 214 pp.
	CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9615127	A1	19960523	WO 1995-GB2613	19951108 <--
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2202135	A1	19960523	CA 1995-2202135	19951108 <--
AU 9538132	A	19960606	AU 1995-38132	19951108 <--
AU 705938	B2	19990603		
EP 790996	A1	19970827	EP 1995-936046	19951108 <--
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CN 1171787	A	19980128	CN 1995-197220	19951108 <--
CN 1067685	B	20010627		
JP 10508617	T	19980825	JP 1995-515817	19951108 <--
AT 215085	T	20020415	AT 1995-936046	19951108 <--
FI 9701971	A	19970512	FI 1997-1971	19970507 <--
NO 9702153	A	19970709	NO 1997-2153	19970509 <--
NO 308899	B1	20001113		
US 6214826	B1	20010410	US 1999-365562	19990802 <--
PRIORITY APPLN. INFO.:			GB 1994-22894 A	19941112 <--
			WO 1995-GB2613 W	19951108 <--
			US 1997-836082 B1	19970502 <--
			US 1998-128038 B1	19980803 <--

OTHER SOURCE(S): MARPAT 125:142755

ED Entered STN: 13 Aug 1996

AB **Pyridazinoquinolines** and related compds. I [ring A is an orthofused aromatic or heteroarom. five- or six-membered ring; R = halo, C1-C4 alkyl, NO2, CN, etc.; R1 = H, C1-C6 alkyl, (CH2)nL, where n = 0-6, L = (un)substituted aryl or heteroaryl or n > 0, L = OH, OAc, halo, CF3, etc.; R2 = H, (CH2)nL; R3 = H, acyl, alkyl, etc.; R4n = bond or H2; R5 = H, C1-C6-alkyl or alkylaryl] or pharmaceutical compns. containing them were prepared for the treatment of neurol. disorders. Thus, di-Me 7-chloro-4-hydroxy-2,3-quinolinedicarboxylate was reacted with 2-hydroxyethylhydrazine and the mixture treated with N-methylglucamine to afford 37% 7-chloro-1-hydroxy-3-(2-hydroxyethyl)-3,4,5,10-**tetrahydropyridazino**[4,5-b]quinoline-4,10-dione. The quinolinedicarboxylate substrate was prepared from Me 2-amino-4- chlorobenzoate and di-Me acetylenedicarboxylate. Compds. I reduced ischemic damage, e.g., 7-chloro-4-hydroxy-5,10-dihydro-2-p- **tolylpyridazino**[4,5-b]quinolin-1-one at an i.v. dose of 10 mg/kg/h caused an infarct % volume change of -42% while a 5.0 mg/kg/h i.v. dosage caused a -8% reduction

IC ICM C07D471-04
ICS A61K031-435; C07D471-14; C07D491-147; C07D495-14

ICI C07D471-04, C07D237-00, C07D221-00

CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST **pyridazinoquinoline** aryl prepn treatment neurol disorder; stroke

treatment **pyridazinoquinoline**; quinoline **pyridazino** prepn treatment neurol disorder

IT Brain, disease
(stroke, preparation of **pyridazinoquinolines**)

IT 179543-41-0P 179543-45-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of **pyridazinoquinolines**)

IT 179543-44-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of **pyridazinoquinolines**)

IT 79-03-8, Propionyl chloride 92-54-6, n-Phenylpiperazine 100-52-7, Benzaldehyde, reactions 100-63-0, Phenylhydrazine 102-50-1, 4-Methoxy-2-methylaniline 109-84-2, 2-Hydroxyethylhydrazine 123-75-1, Pyrrolidine, reactions 156-51-4, Phenethylhydrazine sulfate 446-48-0, 2-Fluorobenzyl bromide 615-00-9, 2,4-Dimethylphenylhydrazine 622-88-8, 4-Bromophenylhydrazine hydrochloride 637-60-5, 4-Methylphenylhydrazine hydrochloride 762-42-5, Dimethyl acetylenedicarboxylate 823-85-8, 4-Fluorophenylhydrazine hydrochloride 870-46-2, tert-Butyl carbazate 1073-69-4, 4-Chlorophenylhydrazine 1074-82-4, Potassium phthalimide 1490-25-1, Carbomethoxypropionyl chloride 2243-56-3, 1-Naphthylhydrazine hydrochloride 5900-58-3, Methyl 2-amino-4-chlorobenzoate 6284-40-8, n-Methylglucamine 6329-90-4, 3-Chloro-p-anisidine hydrochloride 6628-77-9, 5-Amino-2-methoxypyridine 13123-92-7, 2,4-Dichlorophenylhydrazine 16726-41-3 19501-58-7, 4-Methoxyphenylhydrazine hydrochloride 19690-59-6 20570-96-1, Benzylhydrazine dihydrochloride 39232-91-2, 3-Methoxyphenylhydrazine hydrochloride 51145-58-5, 4-Benzyloxyphenylhydrazine 57396-67-5, 2-Methoxyphenylhydrazine hydrochloride 58791-94-9 63756-98-9, 3,4-Dimethoxyphenylhydrazine 147494-03-9 147494-49-3 170142-20-8 170143-20-1 170143-35-8 170143-39-2 170143-43-8 170143-56-3 170143-57-4 170143-58-5 170143-59-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **pyridazinoquinolines**)

IT 24630-85-1P, 3-Chloro-4-methoxyphenylhydrazine 93048-16-9P 133115-72-7P, 4-(Trifluoromethoxy)phenylhydrazine hydrochloride 147494-01-7P 160664-95-9P, 5-Hydrazino-2-methoxypyridine 170141-82-9P 170141-88-5P 170141-89-6P 170142-01-5P 170142-12-8P 170142-26-4P 170142-27-5P 170142-28-6P 170142-44-6P 170142-49-1P 170143-21-2P 170143-22-3P 170143-23-4P 170143-25-6P 170143-26-7P 170143-27-8P 170143-28-9P 170143-29-0P 170143-30-3P 170143-31-4P 170143-32-5P 170143-33-6P 170143-34-7P 170143-36-9P 170143-37-0P 170143-38-1P 170143-41-6P 170143-42-7P 170143-44-9P 170143-45-0P 170143-47-2P 170143-48-3P 170143-49-4P 170143-50-7P 170143-51-8P 170143-52-9P 170143-53-0P 170143-61-0P 179543-31-8P 179543-85-2P 179543-86-3P 179543-87-4P 179543-88-5P 179543-89-6P 179543-90-9P 179543-91-0P 179543-92-1P 179543-94-3P 179543-95-4P 179543-96-5P 179543-97-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of **pyridazinoquinolines**)

IT 170141-81-8P 170141-83-0P 170141-84-1P 170141-86-3P 170141-87-4P 170141-90-9P 170141-91-0P 170141-92-1P 170141-93-2P 170141-94-3P 170141-96-5P 170141-97-6P 170141-98-7P 170141-99-8P 170142-00-4P 170142-02-6P 170142-03-7P 170142-04-8P 170142-05-9P 170142-06-0P 170142-07-1P 170142-08-2P 170142-09-3P 170142-10-6P 170142-11-7P 170142-13-9P 170142-14-0P 170142-15-1P 170142-16-2P 170142-17-3P 170142-18-4P 170142-19-5P 170142-21-9P 170142-22-0P 170142-23-1P

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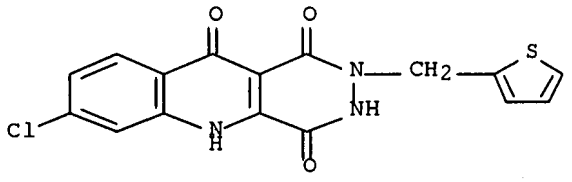
179543-80-7P 179543-81-8P 179543-82-9P 179543-83-0P 179543-84-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of **pyridazinoquinolines**)

IT **170142-52-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of **pyridazinoquinolines**)

RN 170142-52-6 HCAPLUS
CN Pyridazino[4,5-b]quinoline-1,4,10(5H)-trione, 7-chloro-2,3-dihydro-2-(2-thienylmethyl)- (9CI) (CA INDEX NAME)



L99 ANSWER 22 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:685324 HCAPLUS Full-text
DOCUMENT NUMBER: 125:328724
TITLE: Preparation of **dihydropyridazinones** and **pyridazinones** as fungicides and insecticides
INVENTOR(S): Ross, Ronald; Shaber, Steven Howard; Szapacs, Edward Michael
PATENT ASSIGNEE(S): Rohm and Haas Company, USA
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 738716	A2	19961023	EP 1996-302488	19960409 <--
EP 738716	A3	19981230		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
US 5635494	A	19970603	US 1995-426514	19950421 <--
AU 9650550	A	19961031	AU 1996-50550	19960409 <--
AU 713334	B2	19991202		
CA 2174296	A1	19961022	CA 1996-2174296	19960416 <--
TW 499294	B	20020821	TW 1996-85104563	19960417 <--
ZA 9603140	A	19961021	ZA 1996-3140	19960419 <--
JP 08291147	A	19961105	JP 1996-120852	19960419 <--
CN 1143637	A	19970226	CN 1996-104596	19960419 <--
CN 1124267	B	20031015		
HU 9601035	A2	19970428	HU 1996-1035	19960419 <--
BR 9602004	A	19980407	BR 1996-2004	19960419 <--
PRIORITY APPLN. INFO.:			US 1995-426514 A	19950421 <--

OTHER SOURCE(S): MARPAT 125:328724
ED Entered STN: 21 Nov 1996
AB The title compds. [I; W = CH3OA:CC(O)VCH3 (wherein A = N, CH; V = O, NH); X = H, halo, C1-4 alkyl, etc.; Y = O, S, (substituted) NH, etc.; R1 = H, C1-12 alkyl, C1-12 alkoxy, etc.; R2, R3 = H, halo, C1-8 alkyl, etc.; n = 0-1] having fungicidal and insecticidal properties, were prepared Thus, reaction of 6-(3-hydroxyphenyl)-2-(2',2'2'trifluoroethyl)-3(2H)- **pyridazinone** with Me α-(2-bromomethylphenyl)-β- methoxyacrylate in the presence of KOH in DMF afforded the expected **pyridazinone** II which showed 90% or better control when tested against Mexican bean beetle and two-spotted spider mite at 300 g/ha.
IC ICM C07D237-16
ICS C07D237-18; C07D237-20; C07D237-22; A01N043-58
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 5
ST **pyridazinone** prepn fungicide agrochem insecticide; **hydropyridazinone** prepn fungicide agrochem insecticide
IT Insecticides
(preparation of **dihydropyridazinones** and **pyridazinones** as fungicides and insecticides)
IT Fungicides and Fungistats
(agrochem., preparation of **dihydropyridazinones** and **pyridazinones** as fungicides and insecticides)
IT 183233-06-9P 183233-08-1P 183233-09-2P 183233-10-5P 183233-12-7P
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183233-74-1P 183233-75-2P 183233-77-4P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **dihydropyridazinones** and **pyridazinones** as fungicides and insecticides)

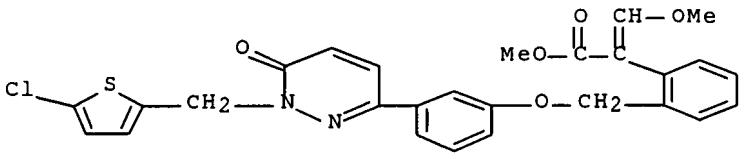
IT 100-39-0, Benzyl bromide 106-94-5, Propyl bromide 108-46-3, Resorcinol, reactions 121-71-1, 3'-Hydroxyacetophenone 141-30-0, 3,6-**Dichloropyridazine** 298-12-4, Glyoxylic acid 107048-59-9 183233-83-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **dihydropyridazinones** and **pyridazinones** as fungicides and insecticides)

IT 147849-75-0P 183233-79-6P 183233-80-9P 183233-81-0P 183233-82-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of **dihydropyridazinones** and **pyridazinones** as fungicides and insecticides)

IT **183233-44-5P**
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **dihydropyridazinones** and **pyridazinones** as fungicides and insecticides)

RN 183233-44-5 HCAPLUS

CN Benzeneacetic acid, 2-[[3-[1-[(5-chloro-2-thienyl)methyl]-1,6-dihydro-6-oxo-3-pyridazinyl]phenoxy]methyl]-α-(methoxymethylene)-, methyl ester (9CI) (CA INDEX NAME)



L99 ANSWER 23 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:909365 HCAPLUS Full-text
DOCUMENT NUMBER: 123:313994
TITLE: Preparation of **pyridazinoquinolines** as NMDA receptor antagonists
INVENTOR(S): Bare, Thomas Michael; Sparks, Richard Bruce; Empfield, James Roy; Davenport, Timothy Wayne; McKinney, Jeffrey Alan
PATENT ASSIGNEE(S): Zeneca Ltd., UK
SOURCE: PCT Int. Appl., 185 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9511244	A1	19950427	WO 1994-GB2295	19941020 <--

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, NL, NO, NZ, PL, PT, RO, RU, SE, SI, SK, TJ, TT, UA, US, UZ, VN
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

IL 111266	A	20020310	IL 1994-111266	19941012	<--
ZA 9408178	A	19950424	ZA 1994-8178	19941018	<--
CA 2171332	A1	19950427	CA 1994-2171332	19941020	<--
AU 9479440	A	19950508	AU 1994-79440	19941020	<--
AU 688393	B2	19980312			
EP 724583	A1	19960807	EP 1994-930275	19941020	<--
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
HU 74161	A2	19961128	HU 1996-889	19941020	<--
CN 1138332	A	19961218	CN 1994-194578	19941020	<--
CN 1053189	B	20000607			
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JP 3583132	B2	20041027			
NZ 329303	A	20000128	NZ 1994-329303	19941020	<--
EP 1004582	A2	20000531	EP 2000-101917	19941020	<--
EP 1004582	A3	20000830			
EP 1004582	B1	20050518			
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AT 198072	T	20001215	AT 1994-930275	19941020	<--
PL 180679	B1	20010330	PL 1994-314041	19941020	<--
PT 724583	T	20010330	PT 1994-930275	19941020	<--
ES 2154686	T3	20010416	ES 1994-930275	19941020	<--
RU 2168511	C2	20010610	RU 1996-109470	19941020	<--
SK 282491	B6	20020205	SK 1996-504	19941020	<--
SG 92630	A1	20021119	SG 1999-943	19941020	<--
CZ 292311	B6	20030917	CZ 1996-1138	19941020	<--
AT 295846	T	20050615	AT 2000-101917	19941020	<--
PT 1004582	T	20050930	PT 2000-101917	19941020	<--
ES 2241513	T3	20051101	ES 2000-101917	19941020	<--
RU 2279432	C2	20060710	RU 2001-103922	19941020	<--
TW 406082	B	20000921	TW 1994-83110721	19941118	<--
US 5744471	A	19980428	US 1996-637641	19960417	<--
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NO 9601584	A	19960419	NO 1996-1584	19960419	<--
NO 306995	B1	20000124			
FI 9700907	A	19970303	FI 1997-907	19970303	<--
FI 114916	B1	20050131			
US 6232313	B1	20010515	US 1998-44109	19980319	<--
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AU 721139	B2	20000622			
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US 6103721	A	20000815	US 1999-455096	19991206	<--
GR 3035080	T3	20010330	GR 2000-402690	20001214	<--

PRIORITY APPLN. INFO.:	GB 1993-21854	A	19931022	<--
	GB 1994-17171	A	19940825	<--
	AU 1994-79440	A	19941020	<--
	EP 1994-930275	A3	19941020	<--
	RU 1996-109470	A3	19941020	<--
	WO 1994-GB2295	W	19941020	<--
	US 1996-637641	A3	19960417	<--
	FI 1996-1696	A	19960418	<--
	US 1998-44109	A3	19980319	<--

OTHER SOURCE(S): MARPAT 123:313994

ED Entered STN: 11 Nov 1995

AB Title compds. [(tautomeric) I; A = atoms to complete an (un)substituted benzene, pyridine, furan, pyrrole, or **thiophene** ring; R1,R2 = H, (CH2)nR; R = (un)substituted Ph, -heterocyclyl, -heteroaryl, OH, alkoxy, acyloxy, (di)alkylamino, etc.; R4 = 1 or more halo, alkyl, cyano, alkoxy, etc.; Z = O,

S, NH] were prepared Thus, Me 4-chloroanthranilate was cyclocondensed with MeO2CC.tplbond.CCO2Me and the product cyclocondensed in 2 steps with H2NNHCH2CH2OH to give title compound II (R = OH) which was converted in 2 steps to II (R = phthalimido). II [R = C6H4(OMe)-4] gave 80% protection from brain ischemic damage in carotid artery clip-occluded gerbils at 10mg/kg i.p.

IC ICM C07D471-04
ICS A61K031-50

ICI C07D471-04, C07D237-00, C07D221-00

CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST **pyridazinoquinoline** prepn NMDA receptor antagonist

IT Anticonvulsants and Antiepileptics
(preparation of **pyridazinoquinolines** as NMDA receptor antagonists)

IT Ischemia
(treatment; preparation of **pyridazinoquinolines** as NMDA receptor antagonists)

IT Nervous system
(disease, degeneration, treatment; preparation of **pyridazinoquinolines** as NMDA receptor antagonists)

IT Neurotransmitter antagonists
(excitatory amino acid, preparation of **pyridazinoquinolines** as NMDA receptor antagonists)

IT Neurotransmitter antagonists
(methyl-D-aspartate, **pyridazinoquinolines**)

IT Brain, disease
(stroke, treatment; preparation of **pyridazinoquinolines** as NMDA receptor antagonists)

IT 147494-01-7P 170141-81-8P 170141-82-9P 170141-84-1P 170141-86-3P
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of **pyridazinoquinolines** as NMDA receptor antagonists)

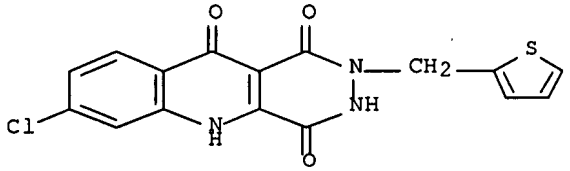
IT 170141-83-0
RL: PRP (Properties)
(preparation of **pyridazinoquinolines** as NMDA receptor antagonists)

IT 92-54-6, N-Phenylpiperazine 100-52-7, Benzaldehyde, reactions 100-63-0, Phenylhydrazine 102-50-1, 2-Methyl-4-methoxyaniline 104-94-9, p-Anisidine 123-75-1, Pyrrolidine, reactions 156-51-4, 2-Phenethylhydrazine sulfate 446-48-0, 2-Fluorobenzyl bromide 615-00-9, 2,4-Dimethylphenylhydrazine 762-42-5, Dimethyl acetylenedicarboxylate 1073-69-4, 4-Chlorophenylhydrazine 1074-82-4, Potassium phthalimide 2243-56-3 5839-88-3, 4,4-Dimethyloxazoline-2,5-dione 5900-58-3, Methyl 2-amino-4-chlorobenzoate 6329-90-4, 3-Chloro-p-anisidine hydrochloride 6628-77-9, 5-Amino-2-methoxypyridine 13123-92-7, 2,4-Dichlorophenylhydrazine 20570-96-1 24424-99-5, Di-tert-butyl dicarbonate 35467-65-3, 4-Methylphenylhydrazine hydrochloride 40594-35-2, 4-Fluorophenylhydrazine hydrochloride 41931-18-4, 4-Bromophenylhydrazine hydrochloride 51145-58-5, 4-Benzyloxyphenylhydrazine 57396-67-5, 2-Methoxyphenylhydrazine hydrochloride 57396-68-6, 3-Methoxyphenylhydrazine hydrochloride 58791-94-9 63756-98-9, 3,4-Dimethoxyphenylhydrazine 70672-74-1, 4-Methoxyphenylhydrazine hydrochloride 118427-29-5, 4-Isopropylphenylhydrazine hydrochloride 133115-72-7, 4-(Trifluoromethoxy)phenylhydrazine hydrochloride 147494-03-9 147494-49-3 170143-56-3 170143-57-4 170143-58-5 170143-59-6 170143-60-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **pyridazinoquinolines** as NMDA receptor antagonists)

IT 13957-54-5P 24630-85-1P, 3-Chloro-4-methoxyphenylhydrazine 93048-16-9P, 2-Methyl-4-methoxyphenylhydrazine hydrochloride 160664-95-9P, 5-Hydrazino-2-methoxypyridine 170143-24-5P 170143-25-6P 170143-26-7P 170143-27-8P 170143-28-9P 170143-29-0P 170143-30-3P 170143-31-4P 170143-32-5P 170143-33-6P 170143-34-7P 170143-35-8P 170143-36-9P 170143-37-0P 170143-38-1P 170143-41-6P 170143-42-7P 170143-43-8P 170143-44-9P 170143-45-0P 170143-47-2P 170143-48-3P 170143-49-4P 170143-50-7P 170143-51-8P 170143-52-9P 170143-53-0P 170143-54-1P 170143-55-2P 170143-61-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of **pyridazinoquinolines** as NMDA receptor antagonists)

IT **170142-52-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of **pyridazinoquinolines** as NMDA receptor antagonists)

RN 170142-52-6 HCAPLUS
CN Pyridazino[4,5-b]quinoline-1,4,10(5H)-trione, 7-chloro-2,3-dihydro-2-(2-thienylmethyl)- (9CI) (CA INDEX NAME)



L99 ANSWER 24 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:52662 HCAPLUS
DOCUMENT NUMBER: 124:176127
TITLE: Preparation of sulfamoylindanyl- and sulfamoyl-1,2,3,4-**tetrahydronaphthylpyridazinone*** ** derivatives as drugs
INVENTOR(S): Ishida, Akihiko; Pponma, Koichi; Kono, Haruyuki; Tamura, Koji; Sasaki, Yasuhiko
PATENT ASSIGNEE(S): Tanabe Seiyaku Co, Japan
SOURCE: Japan Kokai Tokkyo Koho, 35 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
JP 07233072	A	19950905	JP 1994-322942		19941226	<--
PRIORITY APPLN. INFO.:			JP 1994-322942	A	19941226	<--
			JP 1993-333966		19931228	<--

OTHER SOURCE(S): MARPAT 124:176127
ED Entered STN: 26 Jan 1996
AB The title compds. [I; R1 = (un)substituted C1-10 alkyl, C3-6 cycloalkyl, lower alkenyl, (un)substituted heterocyclyl containing N, O, or S heteroatom, camphor-10-yl; R3 = H, (un)substituted lower alkyl, lower alkenyl; or R1 and R3 are linked to each other at the termini to form a lower alkylene; R2 = H, (un)substituted lower alkyl, aryl, lower alkenyl; A-B = ethylene or vinylene optionally substituted by 1-2 groups selected from lower alkyl or Ph; n = 1,2; D = H, halo], which are useful for the treatment and prevention of nephritis, in particular glomerulonephritis, IgA nephritis, nephrotic syndrome, and/or lupus nephritis and as blood platelet aggregation inhibitors and/or protective agents against endotoxin shock, are prepared Thus, 1.15 g 2-amino-5-[3-oxo-3(H)-4,5- **dihydropyridazin**-6-yl]indan was dissolved in EtOAc and THF, followed by successively adding an aqueous solution of 1.4 g K2CO3 in 20 mL and 0.57 g MeSO2Cl, and the resulting mixture was stirred for 2 h to give 1.08 g 2-methanesulfonylamino-5-[3-oxo-3(H)-4,5-**dihydropyridazin** -6-yl]indan (II). Mice was administered with II at 100 mg/kg p.o. and after 30 min treated with a solution of Escherichia coli-derived endotoxin (lipopolysaccharides) in physiol. saline at 100 mg/10 mL/kg i.p. The survival ratio of the treated mice was 100 %.
IC ICM A61K031-50
ICS A61K031-50; C07D237-04; C07D401-12; C07D403-12; C07D409-12; C07D409-14; C07D413-12; C07D417-14
ICI C07D401-12, C07D213-16, C07D237-04; C07D401-12, C07D215-04, C07D237-04; C07D409-12, C07D237-04, C07D333-10; C07D409-14, C07D213-16
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
ST **sulfamoylindanylpyridazinone** prepn treatment nephritis; **sulfamoyltetrahydronaphthylpyridazinone** prepn treatment nephrotic syndrome; glomerulonephritis treatment **sulfamoylindanylpyridazinone*** * ; IgA nephritis treatment ***sulfamoylindanylpyridazinone**; lupus nephritis treatment **sulfamoylindanylpyridazinone**; blood platelet aggregation inhibitor **sulfamoylindanylpyridazinone**; endotoxin shock protection **sulfamoylindanylpyridazinone**; **indanylpyridazinone** sulfamoyl prepn treatment nephritis; **naphthylpyridazinone** sulfamoyl prepn treatment nephrotic syndrome; **pyridazinone** sulfamoyl indanyl prepn treatment nephritis

IT Blood platelet aggregation inhibitors
(preparation of sulfamoylindanyl- and **sulfamoyltetrahydronaphthylpyridazinone** derivs. as drugs)

IT Shock
(endotoxin, preparation of sulfamoylindanyl- and **sulfamoyltetrahydronaphthylpyridazinone** derivs. as drugs for treating nephritis and protecting against endotoxin shock)

IT Kidney, disease
(nephritis, preparation of sulfamoylindanyl- and **sulfamoyltetrahydronaphthylpyridazinone** derivs. as drugs for treating nephritis (glomerulonephritis, IgA nephritis, nephrotic syndrome, and/or lupus nephritis))

IT 155718-08-4P 155718-25-5P 155718-33-5P 155718-34-6P 155718-80-2P
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172680-71-6P 172680-72-7P 172680-73-8P 172680-74-9P 172680-75-0P
172680-76-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfamoylindanyl- and **sulfamoyltetrahydronaphthylpyridazinone** derivs. as drugs)

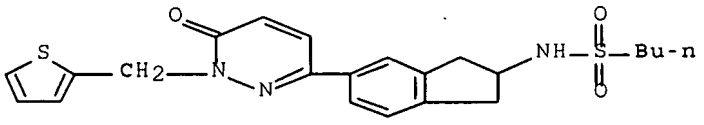
IT 74-88-4, Methyl iodide, reactions 75-36-5, Acetyl chloride 75-86-5, Acetone cyanohydrin 79-30-1, 2-Methylpropanoyl chloride 85-44-9, Phthalic anhydride 96-32-2, Methyl bromoacetate 100-39-0, Benzyl bromide 100-52-7, Benzaldehyde, reactions 103-80-0, Phenylacetyl chloride 105-36-2, Ethyl bromoacetate 106-65-0, Dimethyl succinate 107-08-4, Propyl iodide 107-99-3, 2-Dimethylaminoethyl chloride 108-30-5, Succinic anhydride, reactions 108-90-7, Chlorobenzene, reactions 123-38-6, Propanal, reactions 124-63-0, Methanesulfonyl chloride 677-25-8, Vinylsulfonyl fluoride 1490-25-1, Methyl succinyl chloride 1622-32-8, 2-Chloroethanesulfonyl chloride 1633-82-5, 3-Chloropropanesulfonyl chloride 2386-60-9, n-Butanesulfonyl chloride 2975-41-9, 2-Aminoindan 3099-31-8, 3-Picolyl chloride 3144-16-9, (+)-Camphorsulfonic acid 3878-55-5, Methyl hydrogen succinate 7803-57-8, Hydrazine hydrate 10147-36-1, Propanesulfonyl chloride 16629-19-9, 2-**Thiophenesulfonyl** chloride 79686-90-1, 2-Methoxycarbonylaminosuccinic anhydride 114149-01-8 138006-38-9, 2-Propionylaminoindan 166978-75-2 172679-98-0 172680-84-1 172681-01-5

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of sulfamoylindanyl- and **sulfamoyltetrahydronaphthylpyridazinone** derivs. as drugs)

IT 31952-21-3P 64624-93-7P, 2-Propylindan 155719-25-8P, 2-Butanesulfonylaminoindan 155719-33-8P 155719-35-0P 155719-36-1P 155719-37-2P 155719-41-8P 155719-43-0P 155719-53-2P 155719-54-3P 166978-76-3P 166978-77-4P 166978-78-5P 166978-83-2P 166978-84-3P 166978-85-4P 172680-79-4P 172680-80-7P 172680-81-8P 172680-82-9P 172680-83-0P 172680-85-2P 172680-86-3P 172680-87-4P 172680-88-5P 172680-89-6P 172680-90-9P 172680-91-0P 172680-92-1P 172680-93-2P 172680-94-3P 172680-95-4P 172680-96-5P 172680-97-6P 172680-98-7P 172680-99-8P 172681-00-4P 172681-02-6P 172681-03-7P 172681-04-8P 172681-05-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of sulfamoylindanyl- and **sulfamoyltetrahydronaphthylpyridazinone** derivs. as drugs)

IT **172680-47-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfamoylindanyl- and **sulfamoyltetrahydronaphthylpyridazinone** derivs. as drugs)

RN 172680-47-6 HCAPLUS
CN 1-Butanesulfonamide, N-[5-[1,6-dihydro-6-oxo-1-(2-thienylmethyl)-3-pyridazinyl]-2,3-dihydro-1H-inden-2-yl]- (9CI) (CA INDEX NAME)



L99 ANSWER 25 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:257968 HCAPLUS Full-text
DOCUMENT NUMBER: 122:31542
TITLE: Preparation of 1-arylsulfonyl, arylcabonyl and 1-arylphosphonyl-3-phenyl-1,4,5,6-**tetrahydropyridazine** progestin agonists
INVENTOR(S): Combs, Donald W.
PATENT ASSIGNEE(S): Ortho Pharma Corp., USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9401412	A1	19940120	WO 1993-US6394	19930701 <--
W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SE, SK, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, BG, CI, CM, GA, GN				
AU 9346670	A	19940131	AU 1993-46670	19930701 <--

AU 668206	B2	19960426			
EP 650480	A1	19950503	EP 1993-917006	19930701	<--
EP 650480	B1	20011121			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
HU 68424	A2	19950628	HU 1994-3841	19930701	<--
JP 07508987	T	19951005	JP 1993-503486	19930701	<--
BR 9306661	A	19981208	BR 1993-6661	19930701	<--
AT 209189	T	20011215	AT 1993-917006	19930701	<--
PT 650480	T	20020328	PT 1993-917006	19930701	<--
ES 2168276	T3	20020616	ES 1993-917006	19930701	<--
US 5684151	A	19971104	US 1995-362476	19950306	<--
PRIORITY APPLN. INFO.:			US 1992-906984 A2	19920701	<--
			US 1993-80986 A2	19930621	<--
			WO 1993-US6394 W	19930701	<--

OTHER SOURCE(S): MARPAT 122:31542
ED Entered STN: 22 Dec 1994
AB The title compds. [I; A = Q1, Q2; R1 = halogen, CF3, NO2; R3 = H, C1-6 (un)branched alkyl, halogen, CF3; R5 = H, Me; W = direct bond, CH:CH; R1R1 = CH:CHCH:CH], useful as contraceptives and in the treatment of osteoporosis, and which bind to the GABAA receptor, are prepared Thus, **tetrahydropyridazine** II (m.p. 148-149°) was prepared and demonstrated a IC50 (i.e., binding affinity for the rabbit uterus progestin receptor) of 5.3 nM.
IC C07D237-04; C07D409-04; C07F096-509; A61K031-50
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
ST **arylphosphonylphenyltetrahydropyridazine** prepn progestin agonist; osteoporosis treatment prepn **arylphosphonylphenyltetrahydropyridazine**; GABA receptor binding **arylphosphonylphenyltetrahydropyridazine**; **arylsulfonylphenyltetrahydropyridazine** progestin agonist; contraceptive prepn **arylsulfonylphenyltetrahydropyridazine****
IT **Osteoblast**
(1-arylsulfonyl, arylcabonyl and 1-arylphosphonyl-3-phenyl-1,4,5,6-*tetrahydropyridazine** progestin agonists for stimulation of)
IT Osteoporosis
(1-arylsulfonyl, arylcabonyl and 1-arylphosphonyl-3-phenyl-1,4,5,6-**tetrahydropyridazine** progestin agonists for treatment of)
IT Contraceptives
(1-arylsulfonyl, arylcabonyl and 1-arylphosphonyl-3-phenyl-1,4,5,6-**tetrahydropyridazines**)
IT Progestogen receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of 1-arylsulfonyl, arylcabonyl and 1-arylphosphonyl-3-phenyl-1,4,5,6-**tetrahydropyridazine** as agonists of)
IT Neurotransmitter agonists
Neurotransmitter antagonists
(GABAergicA, 1-arylsulfonyl, arylcabonyl and 1-arylphosphonyl-3-phenyl-1,4,5,6-**tetrahydropyridazines**)
IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(progestogen, preparation of 1-arylsulfonyl, arylcabonyl and 1-arylphosphonyl-3-phenyl-1,4,5,6-**tetrahydropyridazine** as agonists of)
IT 159797-68-9 159797-79-2 159797-89-4 159798-05-7 159798-06-8
159798-07-9 159798-08-0 159798-43-3 159798-61-5 159798-69-3
159798-78-4 159798-82-0 159798-88-6 159798-99-9 159799-45-8
159799-87-8 159799-89-0 159799-91-4 159799-93-6 159799-98-1
159800-01-8 159800-03-0 159800-33-6 159800-34-7 159800-35-8

159800-38-1 159800-39-2 159800-44-9 159800-45-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed compound; preparation of 1-arylsulfonyl, arylcabonyl and 1-arylphosphonyl-3-phenyl-1,4,5,6-**tetrahydropyridazine** progestin agonists)

IT 57-83-0, Pregn-4-ene-3,20-dione, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of 1-arylsulfonyl, arylcabonyl and 1-arylphosphonyl-3-phenyl-1,4,5,6-**tetrahydropyridazine** as agonists of)

IT 77-73-6, Dicyclopentadiene 95-13-6, Indene 98-61-3, 4-Iodobenzenesulfonyl chloride 98-88-4, Benzoyl chloride 108-30-5, Succinic anhydride, reactions 378-77-8, Sodium pentafluoropropionate 527-69-5, 2-Furoyl chloride 532-27-4, α-Chloroacetophenone 542-92-7, Cyclopentadiene, reactions 672-75-3, 3-Bromo-4-fluorobenzoyl chloride 824-72-6, Phenylphosphonic dichloride 931-57-7, 1-Methoxycyclohexene 1003-09-4, 2-**Bromothiophene** 1576-35-8, 4-Toluenesulfonyl hydrazide 2751-27-1 3024-72-4, 3,4-Dichlorobenzoyl chloride 3140-93-0, 2,3-**Dibromothiophene** 3984-34-7, 3-(4-Chlorobenzoyl)propionic acid 4083-64-1, Tosyl isocyanate 5271-67-0, 2-**Thiophenecarbonyl** chloride 6335-44-0 15988-11-1 18523-22-3, 2,3'-Dibromoacetophenone 52240-00-3 159797-68-9 159797-71-4 159798-04-6 159798-06-8 159798-97-7 159798-98-8 159799-02-7 159799-10-7 159799-11-8 159799-15-2 159799-45-8 159799-85-6 159800-18-7 159800-62-1 159800-64-3 159800-65-4 159800-69-8 159800-73-4 159800-74-5 159800-75-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 1-arylsulfonyl, arylcabonyl and 1-arylphosphonyl-3-phenyl-1,4,5,6-**tetrahydropyridazine** as progestin agonists)

IT 1011-46-7P 1017-06-7P 1079-73-8P 2166-13-4P 24734-44-9P 29681-94-5P 36725-34-5P 52239-89-1P 52239-91-5P 52239-99-3P 62903-37-1P 66548-93-4P 66549-42-6P 74190-69-5P 92148-77-1P 92244-97-8P 99070-42-5P 103853-58-3P 117278-79-2P 136912-43-1P 136912-47-5P 144028-82-0P 152342-93-3P 159800-46-1P 159800-47-2P 159800-48-3P 159800-49-4P 159800-50-7P 159800-51-8P 159800-52-9P 159800-53-0P 159800-54-1P 159800-55-2P 159800-56-3P 159800-57-4P 159800-58-5P 159800-59-6P 159800-60-9P 159800-61-0P 159800-63-2P 159800-66-5P 159800-67-6P 159800-68-7P 159800-70-1P 159800-71-2P 159800-72-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1-arylsulfonyl, arylcabonyl and 1-arylphosphonyl-3-phenyl-1,4,5,6-**tetrahydropyridazine** as progestin agonists)

IT 71094-17-2P 109809-47-4P 159797-68-9P 159797-69-0P 159797-70-3P 159797-71-4P 159797-72-5P 159797-73-6P 159797-74-7P 159797-75-8P 159797-76-9P 159797-77-0P 159797-78-1P 159797-79-2P 159797-80-5P 159797-81-6P 159797-82-7P 159797-83-8P 159797-84-9P 159797-85-0P 159797-86-1P 159797-87-2P 159797-88-3P 159797-89-4P 159797-90-7P 159797-91-8P 159797-92-9P 159797-93-0P 159797-94-1P 159797-95-2P 159797-96-3P 159797-97-4P 159797-98-5P 159797-99-6P 159798-00-2P 159798-01-3P 159798-02-4P 159798-03-5P 159798-04-6P 159798-05-7P 159798-06-8P 159798-07-9P 159798-08-0P 159798-09-1P 159798-10-4P 159798-11-5P 159798-12-6P 159798-13-7P 159798-14-8P 159798-15-9P 159798-16-0P 159798-17-1P 159798-18-2P 159798-19-3P 159798-20-6P 159798-21-7P 159798-22-8P 159798-23-9P 159798-24-0P 159798-25-1P 159798-26-2P 159798-27-3P 159798-28-4P 159798-29-5P 159798-30-8P 159798-31-9P 159798-32-0P 159798-33-1P 159798-34-2P 159798-35-3P 159798-36-4P 159798-37-5P 159798-38-6P 159798-39-7P 159798-40-0P 159798-41-1P 159798-42-2P 159798-43-3P 159798-44-4P 159798-45-5P 159798-46-6P 159798-47-7P 159798-48-8P 159798-49-9P 159798-50-2P

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159799-96-9P 159799-97-0P 159799-98-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-arylsulfonyl, arylcabonyl and 1-arylphosphonyl-3-phenyl-1,4,5,6-**tetrahydropyridazine** progestin agonists)

IT 159799-99-2P 159800-00-7P 159800-01-8P 159800-02-9P 159800-03-0P
159800-04-1P 159800-05-2P 159800-06-3P 159800-07-4P 159800-08-5P
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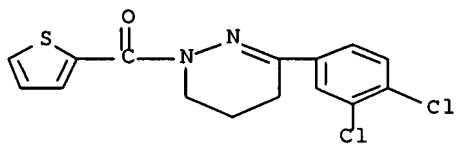
159805-26-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-arylsulfonyl, arylcabonyl and 1-arylphosphonyl-3-phenyl-1,4,5,6-**tetrahydropyridazine** progestin agonists)

IT **159800-21-2P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-arylsulfonyl, arylcabonyl and 1-arylphosphonyl-3-phenyl-1,4,5,6-**tetrahydropyridazine** progestin agonists)

RN 159800-21-2 HCAPLUS
CN Pyridazine, 3-(3,4-dichlorophenyl)-1,4,5,6-tetrahydro-1-(2-thienylcarbonyl)- (9CI) (CA INDEX NAME)



L99 ANSWER 26 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:531213 HCAPLUS Full-text
DOCUMENT NUMBER: 117:131213
TITLE: Preparation of **dihydropyridazinones** and related compounds as fungicides
INVENTOR(S): Egan, Anne Ritchie; Michelotti, Enrique Luis; Ross, Ronald, Jr.; Wilson, Willie Joe
PATENT ASSIGNEE(S): Rohm and Haas Co., USA
SOURCE: Eur. Pat. Appl., 85 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 478195	A1	19920401	EP 1991-308404	19910913 <--
EP 478195	B1	19990526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 180475	T	19990615	AT 1991-308404	19910913 <--
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JP 3408791	B2	20030519		
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CN 1038249	B	19980506		
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US 5552409	A	19960903	US 1994-221229	19940331 <--
US 5631254	A	19970520	US 1995-467384	19950606 <--
US 5753642	A	19980519	US 1995-462472	19950606 <--
US 5726176	A	19980310	US 1996-740546	19961030 <--
US 5726162	A	19980310	US 1996-741248	19961030 <--
US 5728698	A	19980317	US 1996-740548	19961030 <--
US 5728694	A	19980317	US 1996-740549	19961030 <--
US 5728715	A	19980317	US 1996-741249	19961030 <--
JP 2001172264	A	20010626	JP 2000-342863	20001110 <--
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PRIORITY APPLN. INFO.: US 1990-586633 A 19900921 <--
US 1991-749576 A 19910828 <--
JP 1991-241806 A3 19910920 <--
JP 1992-62341 A 19920318 <--
US 1994-221229 A3 19940331 <--
US 1995-467384 A3 19950606 <--

OTHER SOURCE(S): MARPAT 117:131213

ED Entered STN: 04 Oct 1992

AB Title compds. I [A = (CHR2)nCHR7Z, (CHR2)nOZ, (CHR2)nSZ, OCHR7Z, etc.; n = 0-2; D = N, CR2; Q = (substituted) Ph, -naphthyl, -styryl, -pyridyl, -quinolyl, -indolyl, etc.; Z = CO, C:S; R1 = (substituted) alkyl, -alkynyl, -alkenyl, Ph, etc.; R2 = H, C1-3 alkyl, Ph, halo; R7 = R2, alkenylalkenyl, alkynyl, dialkynyl, halolkynyl, alkenylalkynyl; or R2 and R7 form fused Ph ring, etc., with provisos] were prepared as medical and agrochem. fungicides. Thus, 3-(4-chlorobenzoyl)propionic acid (preparation given) in absolute EtOH was refluxed for 3 h with hydrazine and the **dihydropyridazinone** formed was N-alkynylated by 1-bromopent-2-yne to give title compound II. II at 200 ppm gave 99% control of Pyricularia oryzae on rice and at 100 ppm gave 100% control of Candida albicans.

IC ICM C07D237-14
ICS C07D237-26; C07D409-04; C07D273-04; C07D213-26; C07D215-22; C07D243-02; C07D285-18; C07D401-04; C07D403-04; C07D403-06

CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 5

ST **pyridazinone** dihydro prepn fungicide; medical agrochem fungicide **dihydropyridazinone**

IT Fungicides and Fungistats
(**dihydropyridazinones** and related compds.)

IT Fungicides and Fungistats
(agrochem., **dihydropyridazinones** and related compds.)

IT Fungicides and Fungistats
(synergistic, **dihydropyridazinone**-containing compns.)

IT 20072-61-1P 33347-86-3P 35507-89-2P 38958-82-6P 38958-84-8P
52239-79-9P 142027-09-6P 142027-10-9P 142027-11-0P 142027-12-1P
142027-13-2P 142027-14-3P 142027-15-4P 142027-16-5P 142027-17-6P
142027-18-7P 142027-19-8P 142027-20-1P 142027-21-2P 142027-22-3P
142027-23-4P 142027-24-5P 142027-25-6P 142027-26-7P 142027-27-8P
142027-28-9P 142027-29-0P 142027-30-3P 142027-31-4P 142027-32-5P
142027-33-6P 142027-34-7P **142027-35-8P** 142027-36-9P
142027-37-0P 142027-38-1P 142027-39-2P 142027-40-5P 142027-41-6P
142027-42-7P 142027-43-8P 142027-44-9P 142027-45-0P 142027-46-1P
142027-47-2P 142027-48-3P 142027-49-4P 142027-50-7P 142027-51-8P
142027-52-9P 142027-53-0P 142027-54-1P 142027-55-2P 142027-56-3P
142027-57-4P 142027-58-5P 142027-59-6P 142027-60-9P 142027-61-0P
142027-62-1P 142027-63-2P 142027-64-3P 142027-65-4P 142027-66-5P
142027-67-6P 142027-68-7P 142027-69-8P 142027-70-1P 142027-71-2P
142027-72-3P 142027-73-4P 142027-74-5P 142027-75-6P 142027-76-7P
142027-77-8P 142027-78-9P 142027-79-0P 142027-80-3P 142027-81-4P
142027-82-5P 142027-83-6P 142027-84-7P 142027-85-8P 142027-86-9P
142027-87-0P 142027-88-1P 142027-89-2P 142027-90-5P 142027-91-6P
142027-92-7P 142027-93-8P 142027-94-9P 142027-95-0P 142027-96-1P
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142028-02-2P 142028-03-3P 142028-04-4P 142028-05-5P 142028-06-6P
142028-07-7P 142028-08-8P 142028-09-9P 142028-10-2P 142028-11-3P
142028-12-4P 142028-13-5P 142028-14-6P 142028-15-7P 142028-16-8P
142028-17-9P 142028-18-0P 142028-19-1P 142028-20-4P 142028-21-5P
142028-22-6P 142028-23-7P 142028-24-8P 142028-25-9P 142028-26-0P
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142048-48-4P 142048-49-5P 142048-50-8P 142079-87-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as fungicide)

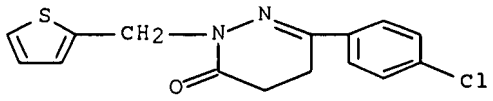
IT 89-41-8P, 3-Nitro-4-methoxybenzoic acid 403-17-8P 664-66-4P
697-20-1P 765-50-4P, 2-**Chloromethylthiophene** 866-16-0P
1079-73-8P 1810-67-9P 2919-05-3P, 4-Penten-2-yn-1-ol 2927-72-2P
3355-28-0P, 1-Bromo-2-butyne 3984-34-7P 4653-13-8P 5381-29-3P
13280-03-0P 18350-44-2P 19927-64-1P 25445-82-3P 26673-31-4P
27956-39-4P 27993-56-2P, 4-Chloro-α-hydroxyacetophenone
35982-98-0P 41345-53-3P, 2,4-Pentadiyn-1-ol 42134-54-3P 50597-19-8P
50677-27-5P 52157-57-0P, 2-Chloromethyl-5-methylfuran 52240-20-7P
53691-91-1P 55631-84-0P 61493-85-4P 62903-05-3P 62903-14-4P
64244-47-9P 65738-56-9P 69676-55-7P 70391-14-9P 76053-43-5P
77028-10-5P 84314-04-5P 87427-66-5P 87428-49-7P 127941-47-3P
130922-04-2P 130922-09-7P 142048-51-9P 142048-52-0P 142048-53-1P
142048-54-2P 142048-55-3P 142048-56-4P 142048-57-5P 142048-58-6P
142048-59-7P 142048-60-0P 142048-61-1P 142048-62-2P 142048-63-3P
142048-64-4P 142048-65-5P 142048-66-6P 142048-67-7P 142048-68-8P
142048-69-9P 142048-70-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for fungicides)

IT 50-00-0, Formaldehyde, reactions 59-88-1, Phenylhydrazine hydrochloride
60-34-4, Methyl hydrazine 64-17-5, Ethanol, reactions 64-18-6, Formic acid, reactions 67-56-1, Methanol, reactions 68-12-2, reactions
74-96-4, Bromoethane 75-07-0, Acetaldehyde, reactions 75-21-8, Oxirane, reactions 90-60-8, 3,5-Dichlorosalicylaldehyde 91-20-3, Naphthalene, reactions 93-10-7, 2-Quinolinecarboxylic acid 95-50-1, 1,2-Dichlorobenzene 96-32-2, Methyl bromoacetate 98-88-4, Benzoylchloride 99-91-2 100-39-0, Benzyl bromide 102-92-1, Cinnamoyl chloride 104-88-1, 4-Chlorobenzaldehyde, reactions 105-36-2, Ethyl bromoacetate 106-47-8, 4-Chloroaniline, reactions 106-65-0, Dimethyl succinate 106-96-7, Propargyl bromide 107-19-7, Propargyl alcohol
107-91-5, Cyanoacetamide 108-24-7, Acetic anhydride 108-30-5, Succinic anhydride, reactions 108-90-7, Chlorobenzene, reactions 109-50-2, 3-Hexyn-2-ol 109-69-3, Butyl chloride 110-65-6, 2-Butyne-1,4-diol
110-87-2, 3,4-Dihydro-2H-pyran 121-90-4, 3-Nitrobenzoyl chloride
122-01-0, 4-Chlorobenzoyl chloride 123-54-6, 2,4-Pentanedione, reactions
123-76-2 124-38-9, Carbon dioxide, reactions 124-63-0, Methanesulfonyl chloride 147-71-7, D-Tartaric acid 298-12-4, Glyoxylic acid
302-01-2, Hydrazine, reactions 350-28-7 393-52-2, 2-Fluorobenzoyl chloride 455-86-7, 3,4-Difluorobenzoic acid 536-38-9 536-40-3
541-16-2, Di-tert-butyl malonate 541-41-3, Ethyl chloroformate
590-14-7, 1-Bromo-1-propene 590-17-0, Bromoacetonitrile 593-66-8, Vinyl iodide 598-23-2, 3-Methylbutyne 609-65-4, 2-Chlorobenzoyl chloride 616-38-6, Dimethylcarbonate 618-46-2, 3-Chlorobenzoyl chloride 624-65-7, Propargyl chloride 627-15-6, 1,3-Dibromo-1-propene
636-72-6, 2-**Thiophenemethanol** 637-87-6 689-97-4,
Vinylacetylene 697-17-6 699-30-9, Perfluorosuccinic anhydride

764-01-2, 2-Butyn-1-ol 764-60-3, 2-Hexyn-1-ol 766-80-3, 3-Chlorobenzyl bromide 821-10-3, 1,4-Dichloro-2-butyne 917-92-0, 3,3-Dimethyl-1-butyne 931-48-6, Cyclohexylacetylene 933-88-0, 2-Methylbenzoyl chloride 1007-16-5, 3-Bromo-4-fluorobenzoic acid 1128-05-8 1461-22-9, Tributyltin chloride 1501-05-9, 4-Benzoylbutyric acid 1504-58-1, 3-Phenyl-2-propyn-1-ol 1711-05-3, 3-Methoxybenzoyl chloride 1711-06-4, 3-Methylbenzoyl chloride 1711-07-5, 3-Fluorobenzoyl chloride 1711-11-1, 3-Cyanobenzoyl chloride 1878-66-6, 4-Chlorophenylacetic acid 2166-13-4 2219-66-1, 1,4-Dibromo-2-butyne 2251-65-2, 3-Trifluoromethylbenzoyl chloride 2810-04-0, Ethyl 2-**thiophenecarboxylate** 2905-65-9, Methyl 3-chlorobenzoate 3437-95-4, 2-**Iodothiophene** 4100-80-5, Methyl succinic anhydride 4114-31-2, Ethyl carbazate 4117-14-0, 2-Decyn-1-ol 4468-82-0 4784-77-4, Crotyl bromide 5911-08-0, Chloromethylcyclopropane 6273-45-6 6945-92-2, Ethyl hydrazinoacetate hydrochloride 7151-68-0, 3-Methoxy-4-methylbenzoic acid 7400-27-3, tert-Butylhydrazine hydrochloride 10229-10-4, 3-Pentyn-1-ol 14496-35-6 16400-32-1, 1-Bromo-2-pentyne 17715-00-3 19788-37-5 21615-34-9, 2-Methoxybenzoyl chloride 32137-20-5, 4-Chloro-3-fluorobenzotrifluoride 32315-10-9, Triphosgene 37908-96-6, 3-Chloro-4-methoxybenzoic acid 38002-45-8, 1-Bromo-3-trimethylsilyl-2-propyne 40757-20-8 41715-02-0 42348-86-7 52323-98-5 54369-44-7 54745-92-5, 2-Quinoxalinecarbonyl chloride 60811-18-9 66248-97-3 81159-43-5 91085-56-2 142048-71-3 142048-72-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of fungicides)

IT **142027-35-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as fungicide)

RN 142027-35-8 HCAPLUS
CN 3(2H)-Pyridazinone, 6-(4-chlorophenyl)-4,5-dihydro-2-(2-thienylmethyl)- (9CI) (CA INDEX NAME)



L99 ANSWER 27 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:656193 HCAPLUS Full-text
DOCUMENT NUMBER: 115:256193
TITLE: Preparation of fused **pyridazine** derivatives as thromboxane A2 (TXA2) synthetase inhibitors
INVENTOR(S): Ohi, Nobuhiro; Kuroki, Toshio; Yamaguchi, Masahisa; Akima, Michitaka; Koga, Takaki; Kamei, Kenshi
PATENT ASSIGNEE(S): Chugai Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9112251	A1	19910822	WO 1991-JP210	19910219 <--
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
AU 9172381	A	19910903	AU 1991-72381	19910219 <--
ZA 9101224	A	19911127	ZA 1991-1224	19910219 <--
JP 3120857	B2	20001225	JP 1991-504019	19910219 <--
PRIORITY APPLN. INFO.:			JP 1990-37966 A	19900219 <--
			JP 1990-250934 A	19900920 <--
			JP 1990-304547 A	19901109 <--
			JP 1990-409169 A	19901228 <--
			WO 1991-JP210 A	19910219 <--

OTHER SOURCE(S): MARPAT 115:256193

ED Entered STN: 14 Dec 1991

AB Title compds. [I; ring A = Q, or unsatd. 5- or 6-membered O-, N- or S-containing heterocycle, e.g. Q1, Q2; R1 = H, halo CO2H, alkoxycarbonyl, NO2, alkoxy; R2 = alkyl; cyclohexyl, (halo)benzyl, thienylmethyl, (halo or alkyl) unsatd. 5- or 6-membered heterocyclyl containing 1-3 N atoms and/or 1 S atom, (un)substituted Ph; R3 = (un)substituted alkyl, alkenyl, alkynyl, aralkyl, cycloalkyl, cycloalkylmethyl, acyl, acylmethyl, PhSO2], useful as antiasthmatics and bronchodilators, are prepared Thus, a suspension of 4-phenyl-1-(2H)-phthalazinone 2.0, BrCH2CH2Br 5.5, K2CO3 7.5 g, and 60 mL DMF was stirred 2 h at 65° and thereto 4.3 g imidazole was added and the stirring was continued 5 h at 70° to give 0.5g a phthalazinone [II; R2 = Ph, R3 = 2-(1-imidazolyl)ethyl]. II (R2 = 3-pyridyl, R3 = 2-cyclohexylmethyl) in vitro inhibited 99% TXA2 in a test using rabbit blood platelets and porcine aorta microsomes and showed muscle relaxant activity in guinea pig trachea with -log[EC50] of 6.68. A total of 118 I were prepared and similarly tested.

IC ICM C07D401-04
ICS C07D401-14; C07D403-04; C07D403-06; C07D403-14; C07D405-04; C07D405-14; C07D409-04; C07D409-14; C07D417-04; C07D417-14; C07D471-04; C07D495-04; A61K031-50; C12N009-99

CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 7

ST fused **pyridazine** prepn antiasthmatic; bronchodilator fused **pyridazine**; thromboxane A2 synthetase inhibitor; phthalazinone antiasthmatic bronchodilator; **thienopyridazine** antiasthmatic bronchodilator; **pyridinopyridazinone** antiasthmatic bronchodilator

IT Bronchodilators
(phthalazinone, **thienopyridazinone**, and **pyridopyridazinone** derivs.)

IT Bronchodilators
(antiasthmatics, phthalazinone, **thienopyridazinone**, and **pyridopyridazinone** derivs.)

IT 60832-04-4, Thromboxane A2 synthetase
RL: USES (Uses)
(inhibitors, phthalazinone, **thienopyridazinone**, and **pyridopyridazinone** derivs.)

IT 7028-73-1P 137382-05-9P 137382-06-0P 137382-07-1P 137382-08-2P 137382-09-3P 137382-31-1P 137382-32-2P 137382-33-3P 137382-34-4P 137382-35-5P 137382-36-6P 137382-37-7P 137382-38-8P 137382-39-9P 137382-57-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for thromboxane A2 synthetase inhibitor fused **pyridazinone** derivative)

IT 137381-08-9P 137381-09-0P 137381-10-3P 137381-11-4P 137381-12-5P 137381-13-6P 137381-14-7P 137381-15-8P 137381-16-9P 137381-17-0P

137381-18-1P 137381-19-2P 137381-20-5P 137381-21-6P 137381-22-7P
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137381-33-0P 137381-34-1P 137381-35-2P 137381-36-3P 137381-37-4P
137381-38-5P 137381-39-6P 137381-40-9P 137381-41-0P 137381-42-1P
137381-43-2P 137381-44-3P 137381-45-4P 137381-46-5P 137381-47-6P
137381-48-7P 137381-49-8P 137381-50-1P 137381-51-2P 137381-52-3P
137381-53-4P 137381-54-5P 137381-55-6P 137381-56-7P 137381-57-8P
137381-58-9P 137381-59-0P 137381-60-3P 137381-61-4P 137381-62-5P
137381-63-6P 137381-64-7P 137381-65-8P 137381-66-9P 137381-67-0P
137381-68-1P 137381-69-2P 137381-70-5P 137381-71-6P 137381-72-7P
137381-73-8P 137381-74-9P 137381-75-0P 137381-76-1P 137381-77-2P
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137381-98-7P 137381-99-8P 137382-00-4P **137382-01-5P**
137382-02-6P 137382-03-7P 137382-04-8P 137382-10-6P 137382-11-7P
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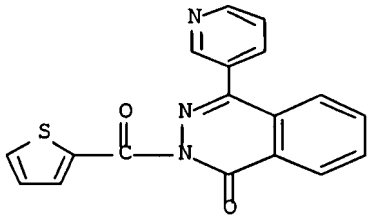
137382-22-0P 137382-23-1P 137382-24-2P 137382-25-3P 137382-26-4P
137382-27-5P 137382-28-6P 137382-29-7P 137382-30-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as thromboxane A2 synthetase inhibitor)

IT 60-34-4, Methylhydrazine 74-88-4, Methyl iodide, reactions 74-96-4, Ethyl bromide 85-44-9, 1,3-Isobenzofurandione 88-65-3, 2-Bromobenzoic acid 95-46-5, 2-Bromotoluene 100-54-9, 3-Cyanopyridine 100-68-5, Thioanisole 106-93-4, 1,2-Dibromoethane 109-64-8, 1,3-Dibromopropane 110-52-1, 1,4-Dibromobutane 111-24-0, 1,5-Dibromopentane 137-43-9, Cyclopentyl bromide 288-32-4, Imidazole, reactions 288-47-1, **Thiazole** 288-88-0, (1H)-1,2,4-Triazole 353-83-3, 2,2,2-Trifluoroethyl iodide 626-55-1, 3-Bromopyridine 627-42-9, 2-Methoxyethyl chloride 629-03-8, 1,6-Dibromohexane 630-17-1, 2,2-Dimethylpropyl bromide 872-31-1, 3-**Bromothiophene** 1766-63-8 2219-66-1, 1,4-Dibromo-2-butyne 3034-53-5, 2-**Bromothiazole** 3140-93-0, 2,3-**Dibromothiophene** 4549-32-0, 1,8-Dibromooctane 4595-59-9, 5-Bromopyrimidine 4752-10-7, 1,4-Dichlorophthalazine 5004-45-5, 4-Phenyl-1-(2H)-phthalazinone 5004-48-8, 4-Methyl-1-(2H)-phthalazinone 6164-79-0, Methyl 2-pyrazinecarboxylate 6974-12-5, 1,4-Dibromo-2-butene 7803-57-8, Hydrazine hydrate 18162-48-6, tert-Butyldimethylsilyl chloride 19487-16-2 19686-73-8, 2-Hydroxypropyl bromide 35541-75-4, 1,4-Bis(bromomethyl)cyclohexane 38254-49-8 51334-85-1 51334-86-2 53242-88-9 57353-93-2 75884-68-3 94614-83-2, 1-(2-Bromoethyl)imidazole 97694-84-3 101351-07-9 102990-37-4 102990-38-5 120116-65-6, 6-Chloro-4-phenyl-1-(2H)-phthalazinone 136610-31-6 136610-32-7 137381-15-8 137382-40-2 137382-41-3 137382-42-4 137382-43-5 137382-44-6 137382-45-7 137382-46-8 137382-47-9 137382-48-0 137382-49-1 137382-50-4 137382-51-5 137382-52-6 137382-53-7 137382-54-8 137382-55-9 137382-56-0 137382-58-2 137382-59-3 137382-60-6 137382-61-7 137382-62-8 137382-63-9 137382-64-0 137382-65-1 137401-47-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of thromboxane A2 synthetase inhibitor fused **pyridazinone** derivative)

IT **137382-01-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as thromboxane A2 synthetase inhibitor)

RN 137382-01-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3-pyridinyl)-2-(2-thienylcarbonyl)- (9CI) (CA

INDEX NAME)



L99 ANSWER 28 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:81862 HCAPLUS Full-text
DOCUMENT NUMBER: 114:81862
TITLE: Preparation of heterocyclic oxophthalazinylacetic acids as aldose reductase inhibitors
INVENTOR(S): Larson, Eric R.; Mylari, Banavara L.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 21 pp. Cont.-in-part of U.S. Ser. No. 136,179.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
US 4939140	A	19900703	US 1988-263577		19881027	<--
CA 1299178	C	19920421	CA 1986-520609		19861016	<--
DD 254001	A5	19880210	DD 1986-296012		19861106	<--
ZA 8608450	A	19880629	ZA 1986-8450		19861106	<--
PRIORITY APPLN. INFO.:			US 1985-796039	B2	19851107	<--
			US 1986-916127	B2	19861007	<--
			US 1987-136179	A2	19871221	<--

OTHER SOURCE(S): MARPAT 114:81862
ED Entered STN: 09 Mar 1991
AB The title compds. I [X = O, S; Z = covalent bond, O, S, NH, CH2, or CHR5Z = vinylene; R1 = OH, prodrug group; R2 = (substituted) (benzo-fused) 5- or 6-membered heterocyclyl, (substituted) imidazolopyridyl, triazolopyridyl, etc.; R3, R4 = H, F, Cl, Br, CF3, alkyl, alkoxy, etc.; or R3R4 = alkylenedioxy; R5 = H, Me, CF3] were prepared I are useful as aldose reductase inhibitors (no data). To a mixture of Et 4-oxo-(3H)-phthalazin-1- ylacetate and NaH in DMF was added 2-(bromomethyl)quinoline. The resulting solution was stirred at room temperature for 30 min to give a product, which was saponified to give, after workup, I [X = O, R1 = OH, R3 = R4 = H, CHR5ZR2 = (quinolin-2-yl)methyl].
IC ICM C07D237-32
ICS C07D519-00; A61K031-50
INCL 514222.00
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 7
IT 942-06-3P, 4,5-Dichlorophthalic anhydride 1772-01-6P 2941-71-1P 4146-24-1P 4760-35-4P 25947-13-1P 40067-66-1P 41014-41-9P 50638-17-0P 50710-33-3P 50737-32-1P 50739-39-4P 51802-77-8P

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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of aldose reductase inhibitor)

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131337-54-7P 131337-55-8P 131337-56-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as aldose reductase inhibitor)

IT **131337-82-1P** **131337-83-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of aldose reductase inhibitor)

RN 131337-82-1 HCAPLUS
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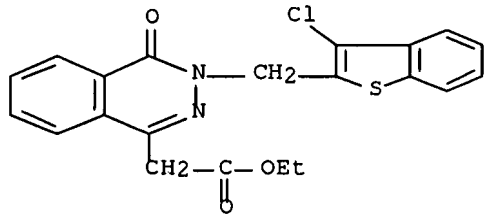

RN 131337-83-2 HCAPLUS
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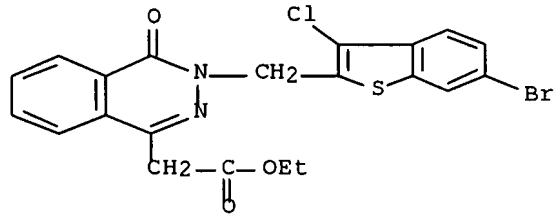

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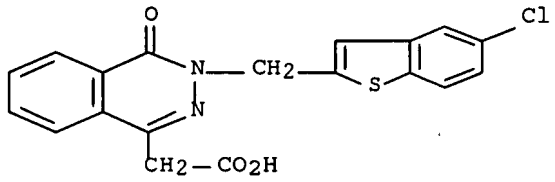
124168-19-0P **124168-20-3P** **124168-21-4P**
124168-23-6P **124168-24-7P** **131337-35-4P**
131337-36-5P **131337-37-6P** **131337-38-7P**
131337-39-8P **131337-40-1P** **131337-48-9P**
131337-49-0P **131337-50-3P** **131337-51-4P**
131337-52-5P **131337-53-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of, as aldose reductase inhibitor)

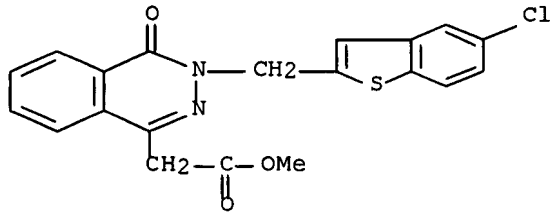
RN 110703-78-1 HCAPLUS

CN 1-Phthalazineacetic acid, 3-[(5-chlorobenzo[b]thien-2-yl)methyl]-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



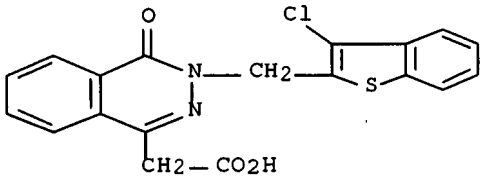
RN 110703-92-9 HCAPLUS

CN 1-Phthalazineacetic acid, 3-[(5-chlorobenzo[b]thien-2-yl)methyl]-3,4-dihydro-4-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 124168-18-9 HCAPLUS

CN 1-Phthalazineacetic acid, 3-[(3-chlorobenzo[b]thien-2-yl)methyl]-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



RN 124168-19-0 HCAPLUS

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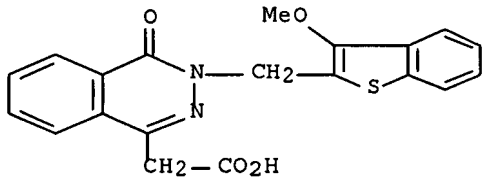

RN 124168-20-3 HCAPLUS
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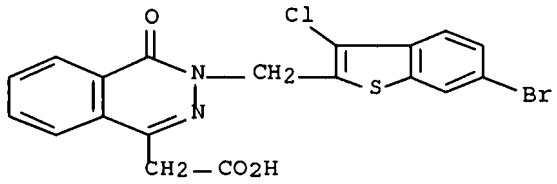

RN 124168-21-4 HCAPLUS
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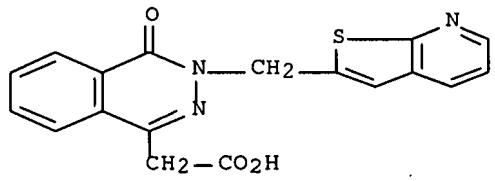

RN 124168-23-6 HCAPLUS
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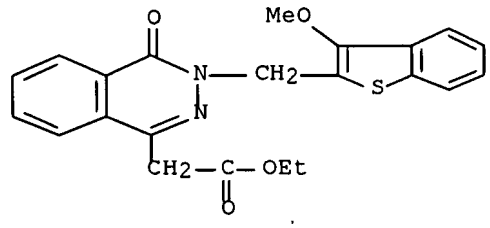

RN 124168-24-7 HCAPLUS
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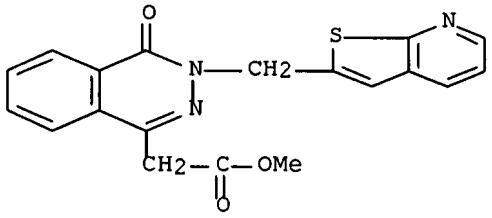
ylmethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 131337-35-4 HCAPLUS
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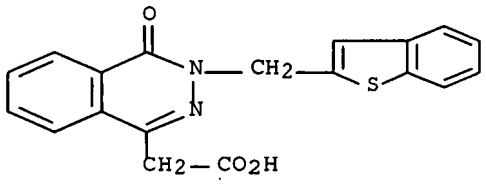

RN 131337-36-5 HCAPLUS
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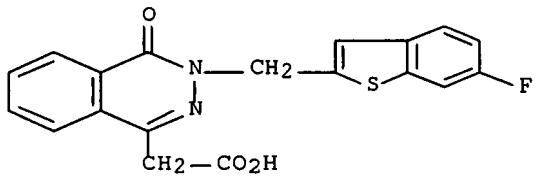

RN 131337-37-6 HCAPLUS
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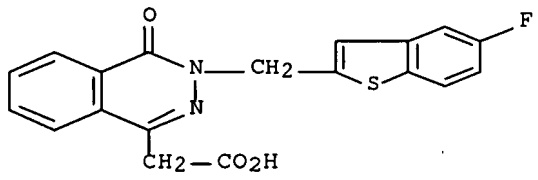

RN 131337-38-7 HCAPLUS
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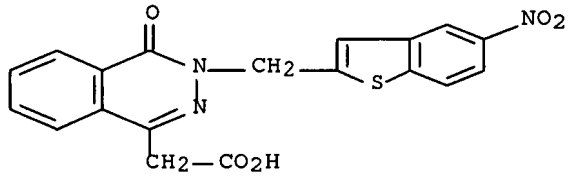

RN 131337-39-8 HCAPLUS
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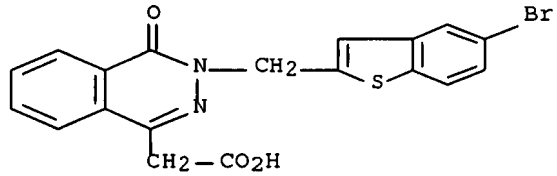

RN 131337-40-1 HCAPLUS
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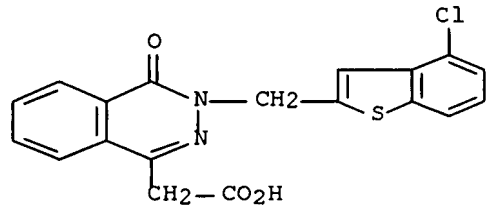

RN 131337-48-9 HCAPLUS
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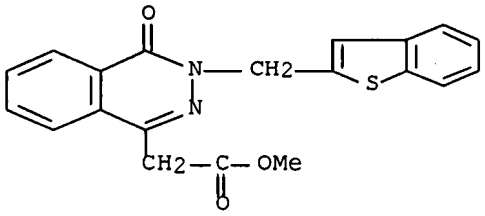

RN 131337-49-0 HCAPLUS
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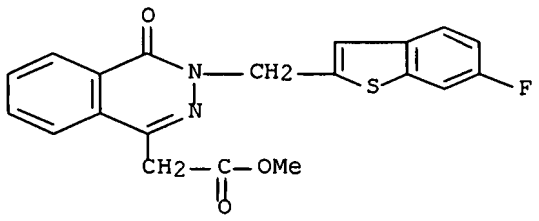

RN 131337-50-3 HCAPLUS
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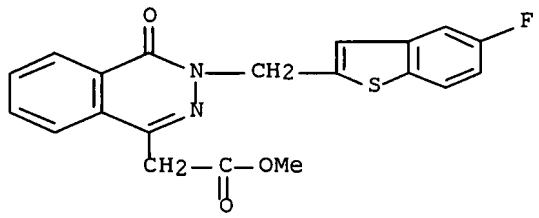

RN 131337-51-4 HCAPLUS
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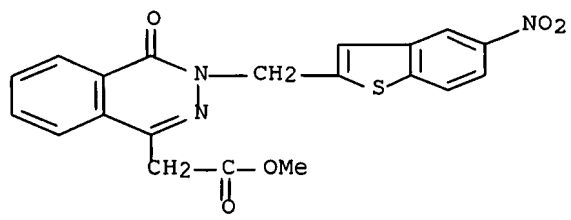

RN 131337-52-5 HCAPLUS
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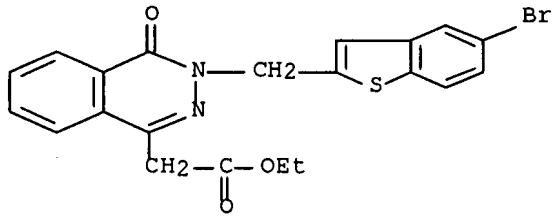

RN 131337-53-6 HCAPLUS
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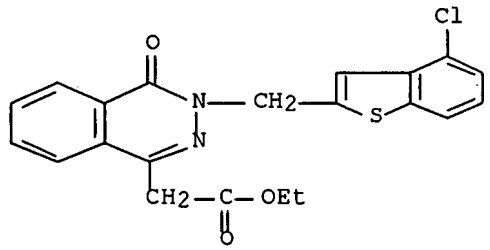

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ACCESSION NUMBER: 1991:164264 HCAPLUS Full-text
DOCUMENT NUMBER: 114:164264
TITLE: Preparation of **pyridopyridazinylacetates** as aldose reductase inhibitors
INVENTOR(S): Mylari, Banavara Lakshmana; Zembrowski, William James
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 401981	A1	19901212	EP 1990-305015	19900510 <--
EP 401981	B1	19950426		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 4996204	A	19910226	US 1989-350417	19890511 <--
CA 2016326	A1	19901111	CA 1990-2016326	19900509 <--
CA 2016326	C	19950530		
NO 9002070	A	19901112	NO 1990-2070	19900510 <--
NO 173938	B	19931115		

NO 173938	C	19940223			
AU 9054905	A	19901115	AU 1990-54905		19900510 <--
AU 611610	B2	19910613			
HU 54683	A2	19910328	HU 1990-2996		19900510 <--
HU 206714	B	19921228			
ZA 9003564	A	19920826	ZA 1990-3564		19900510 <--
FI 93013	B	19941031	FI 1990-2335		19900510 <--
FI 93013	C	19950210			
AT 121743	T	19950515	AT 1990-305015		19900510 <--
ES 2071016	T3	19950616	ES 1990-305015		19900510 <--
JP 03005481	A	19910111	JP 1990-122832		19900511 <--
JP 06031235	B	19940427			

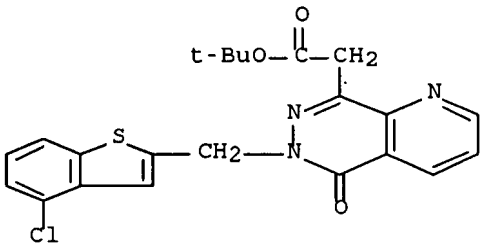
PRIORITY APPLN. INFO.: US 1989-350417 A 19890511 <--
OTHER SOURCE(S): MARPAT 114:164264
ED Entered STN: 03 May 1991
AB The title compds. [I and II; R = H, Me; W = bond, CH2; CRHW = vinyl; X = H, F, Cl, Br, CF3, alkyl, alkoxy, alkylthio; Y = O, S; Z = (substituted) Ph, **thiazolophenyl**, **benzothiophenyl**, benzoxazolyl, **benzothiazolyl**, oxazolopyridinyl, imidazopyridinyl, indolyl, triazolopyridinyl, etc.], and salts and esters thereof, were prepared Thus, tert-Bu 5-oxo-6H-pyrido[2,3-d]**pyridazine**-8-ylacetate (preparation starting from 2,3-pyridinedicarboxylic anhydride and Me3OP2CCH2PPh3 given), KOCMe3, and 2-chloromethyl-5-**trifluoromethylbenzothiazole** were stirred overnight to give 69% coupling product, which was stirred with aqueous H2SO4 to give 53% 6-(5-**trifluoromethylbenzothiazole** -2-ylmethyl)-5-oxo-6H-pyrido[2,3-d]**pyridazin**-8-ylacetic acid. The latter at 10-7 M gave 74% inhibition of aldose reductase in the procedure of S. Hayman.
IC ICM C07D471-04
ICS A61K031-50
ICI C07D471-04, C07D237-00, C07D221-00
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
ST **pyridopyridazinylacetate** prepn aldose reductase inhibitor; **pyridazinylacetate** pyrido aldose reductase inhibitor; cataract treatment **pyridopyridazinylacetate**; retinopathy treatment **pyridopyridazinylacetate**; nephropathy treatment **pyridopyridazinylacetate**; neuropathy treatment **pyridopyridazinylacetate**
IT Diabetes mellitus
(complications from, **pyridopyridazinylacetates** for)
IT Cataract
(treatment of, **pyridopyridazinylacetates**)
IT Eye, disease or disorder
(retinopathy, treatment of, **pyridopyridazinylacetates**)
IT 76283-09-5, 4-Bromo-2-fluorobenzyl bromide 110704-50-2 110704-60-4, 2-Chloromethyl-5-**fluorobenzothiazole** 126764-53-2, 2-Chloromethyl-5,7-**difluorobenzothiazole** 131337-71-8, 4-Chloro-2-**chloromethylbenzothiophene** 133122-57-3, 5-Bromo-2-bromomethylbenzoxazole 133144-89-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with **pyridopyridazinylacetate**, in preparation of aldose reductase inhibitor)
IT 302-01-2, Hydrazine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with (oxopyridofuranylidene)acetate, in preparation of **pyridopyridazinylacetate**)
IT 9028-31-3, Aldose reductase
RL: USES (Uses)
(inhibitors, **pyridopyridazinylacetates**)
IT 131106-55-3P 131666-80-3P 133122-41-5P 133122-42-6P 133122-43-7P

133122-44-8P 133122-45-9P 133122-46-0P 133122-47-1P
133122-48-2P 133122-49-3P 133122-50-6P 133122-51-7P
133122-52-8P 133122-53-9P 133122-54-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as aldose reductase inhibitor)

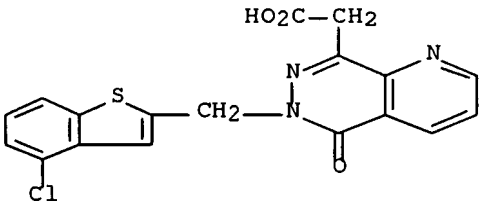
IT 133122-55-1P 133122-56-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for **pyridopyridazinylacetate** aldose reductase inhibitor)

IT **133122-44-8P** **133122-52-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as aldose reductase inhibitor)

RN 133122-44-8 HCAPLUS
CN Pyrido[2,3-d]pyridazine-8-acetic acid, 6-[(4-chlorobenzo[b]thien-2-yl)methyl]-5,6-dihydro-5-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 133122-52-8 HCAPLUS
CN Pyrido[2,3-d]pyridazine-8-acetic acid, 6-[(4-chlorobenzo[b]thien-2-yl)methyl]-5,6-dihydro-5-oxo- (9CI) (CA INDEX NAME)



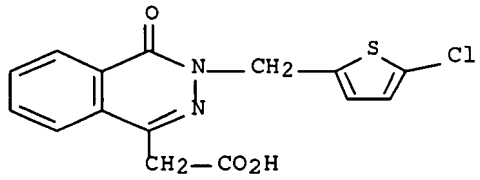
L99 ANSWER 30 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:553824 HCAPLUS Full-text
DOCUMENT NUMBER: 111:153824
TITLE: 5-(4-Oxo-1-phthalazinyl)-2,4-**dioxothiazolidine** derivatives as aldose reductase inhibitors
INVENTOR(S): Niigata, Kunihiro; Okada, Minoru; Yoneda, Takashi
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.

CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

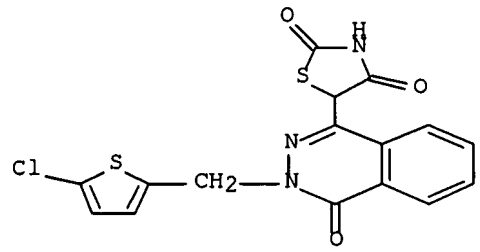
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 01019077	A	19890123	JP 1987-175264	19870713 <--
PRIORITY APPLN. INFO.:			JP 1987-175264	19870713 <--

OTHER SOURCE(S): MARPAT 111:153824
ED Entered STN: 28 Oct 1989
AB Title compds. I [X = H, halo; n = 1,2; R = H, alkyl substituted phenyl-, (halo-substituted)imidazolyl- or thienyl-, naphthyl-, or 2-alkyl-5-**halothiazol**-4-ylalkyl], useful for treatment of diabetic complications such as diseases caused by aldose reductase (no data), are prepared Treatment of a phthalazine II (R1 = CH2CO2Et) (generated in situ from its HBr salt) in CHCl3 with Br in the presence of (PhCO)2O2 under a 300W lamp gave II (R1 = CHBrCO2Et), which in EtOH was refluxed with (H2N)2CS to afford II (R1 = 2,4-**dioxothiazolidin**-5-yl).
IC ICM C07D417-04
ICS A61K031-50; C07D417-14
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
ST **oxophthalazinyldioxothiazolidine** prepn aldose reductase inhibitor; phthalazine **dioxothiazolidinyl** aldose reductase inhibitor; **thiazolidine** phthalazinyl aldose reductase inhibitor
IT Diabetes insipidus
Diabetes mellitus
(complications from, treatment of, by **oxophthalazinyldioxothiazolidine** derivs.)
IT 9028-31-3, Aldose reductase
RL: USES (Uses)
(inhibitors, **oxophthalazinyldioxothiazolidine** derivs. as)
IT 72702-92-2P 122812-84-4P 122812-85-5P 122812-86-6P 122812-87-7P
122812-88-8P 122812-89-9P 122812-90-2P 122812-91-3P
122812-92-4P 122812-93-5P 122812-94-6P 122812-95-7P
122812-96-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of **oxophthalazinyldioxothiazolidine** aldose reductase inhibitors)
IT 122812-67-3P 122812-68-4P 122812-69-5P 122812-70-8P 122812-71-9P
122812-72-0P 122812-73-1P 122812-74-2P 122812-75-3P 122812-76-4P
122812-77-5P **122812-78-6P** 122812-79-7P 122812-80-0P
122812-81-1P 122812-82-2P 122812-83-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as aldose reductase inhibitor)
IT 23784-96-5, 2-Chloro-5-**chloromethylthiophene**
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-alkylation by, of phthalazine derivative)
IT **122812-92-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of **oxophthalazinyldioxothiazolidine** aldose reductase inhibitors)

RN 122812-92-4 HCAPLUS
CN 1-Phthalazineacetic acid, 3-[(5-chloro-2-thienyl)methyl]-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



IT **122812-78-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as aldose reductase inhibitor)
RN 122812-78-6 HCAPLUS
CN 2,4-Thiazolidinedione, 5-[3-[(5-chloro-2-thienyl)methyl]-3,4-dihydro-4-oxo-1-phthalazinyl]- (9CI) (CA INDEX NAME)



L99 ANSWER 31 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:7498 HCAPLUS Full-text
DOCUMENT NUMBER: 112:7498
TITLE: Oxophthalazineacetates as aldose reductase inhibitors
INVENTOR(S): Larson, Eric Robert; Mylari, Banavara Lakshmana
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 322153	A2	19890628	EP 1988-311857	19881215 <--
EP 322153	A3	19900816		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 1299181	C	19920421	CA 1988-586121	19881216 <--
IL 88729	A	19960723	IL 1988-88729	19881219 <--
FI 8805886	A	19890622	FI 1988-5886	19881220 <--

HU 56552	A2	19910930	HU 1988-6506		19881220 <--
HU 207086	B	19930301			
AU 8827337	A	19890622	AU 1988-27337		19881221 <--
AU 609559	B2	19910502			
DK 8807123	A	19890731	DK 1988-7123		19881221 <--
JP 01211585	A	19890824	JP 1988-323225		19881221 <--
JP 06092402	B	19941116			
CN 1035116	A	19890830	CN 1988-109263		19881221 <--
DD 276686	A5	19900307	DD 1988-323606		19881221 <--
ZA 8809519	A	19900829	ZA 1988-9519		19881221 <--
PRIORITY APPLN. INFO.:			US 1987-136179	A	19871221 <--

ED Entered STN: 06 Jan 1990

AB Title compds. I (X = O, S; Z = bond, O, S, NH, CH2; CHR1Z = CH:CH; R1 = OH, groups for prodrug; R2 = heterocyclyl, e.g., imidazolopyridyl, thienopyridyl, and pyrrolyl; R3,R4 = H, F, Cl, Br, CF3, alkyl, alkoxy, alkylsulfonyl, etc.; R3R4 = C1-4 alkylenedioxy; R5 = H, Me, CF3), useful as aldose reductase inhibitors (no data), are prepared Treatment of Et 4-oxo-3H-phthalazin-1-ylacetate in DMF with tert-BuOK and then a **benzothiazole** QCl (R = Me) (preparation given) gave I [R1 = EtO; R3 = R4 = H; X = O; CHR5ZR2 = Q (R = Me)]. Saponification of the latter with aqueous KOH in THF/EtOH, followed by demethylation with HBr gave I (R1 = OH; R = R3 = R4 = H; X = O; CHR5ZR2 = Q).

IC ICM C07D417-06
ICS C07D409-06; C07D471-04; C07D411-06; C07D407-06; C07D403-06; A61K031-50

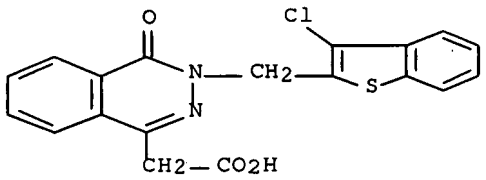
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 110704-61-5P 122665-79-6P 124168-10-1P 124168-11-2P 124168-12-3P
124168-13-4P 124168-14-5P 124168-15-6P 124168-16-7P 124168-17-8P
124168-18-9P **124168-19-0P** **124168-20-3P**
124168-21-4P 124168-22-5P **124168-23-6P**
124168-24-7P 124168-25-8P 124168-26-9P 124168-27-0P
124168-28-1P 124168-29-2P 124168-30-5P 124168-31-6P 124168-32-7P
124168-33-8P 124168-34-9P 124168-35-0P 124168-36-1P 124168-37-2P
124168-38-3P 124168-39-4P 124168-40-7P 124168-41-8P 124168-42-9P
124168-43-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as aldose reductase inhibitor)

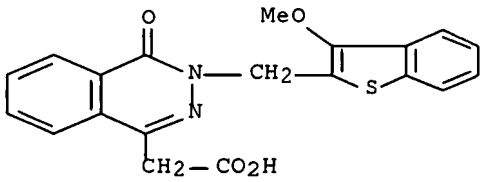
IT **124168-18-9P** **124168-19-0P** **124168-20-3P**
124168-21-4P **124168-23-6P** **124168-24-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as aldose reductase inhibitor)

RN 124168-18-9 HCAPLUS

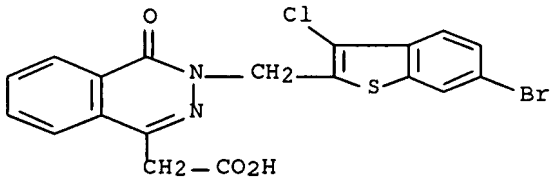
CN 1-Phthalazineacetic acid, 3-[(3-chlorobenzo[b]thien-2-yl)methyl]-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



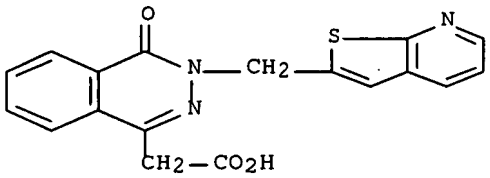
RN 124168-19-0 HCAPLUS
CN 1-Phthalazineacetic acid, 3,4-dihydro-3-[(3-methoxybenzo[b]thien-2-yl)methyl]-4-oxo- (9CI) (CA INDEX NAME)



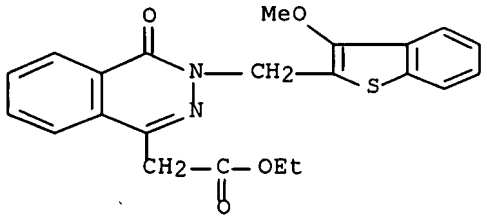
RN 124168-20-3 HCAPLUS
CN 1-Phthalazineacetic acid, 3-[(6-bromo-3-chlorobenzo[b]thien-2-yl)methyl]-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



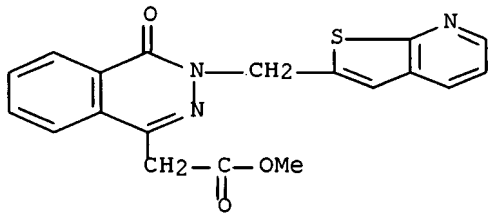
RN 124168-21-4 HCAPLUS
CN 1-Phthalazineacetic acid, 3,4-dihydro-4-oxo-3-(thieno[2,3-b]pyridin-2-ylmethyl)- (9CI) (CA INDEX NAME)



RN 124168-23-6 HCAPLUS
CN 1-Phthalazineacetic acid, 3,4-dihydro-3-[(3-methoxybenzo[b]thien-2-yl)methyl]-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



RN 124168-24-7 HCAPLUS
CN 1-Phthalazineacetic acid, 3,4-dihydro-4-oxo-3-(thieno[2,3-b]pyridin-2-ylmethyl)-, methyl ester (9CI) (CA INDEX NAME)



L99 ANSWER 32 OF 69 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:576055 HCAPLUS Full-text
DOCUMENT NUMBER: 107:176055
TITLE: Preparation of heterocyclic oxophthalazinyl acetic acids derivatives
INVENTOR(S): Mylari, Banavara Lakshmana; Larson, Eric Robert; Zembrowski, William James
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 41 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 222576	A2	19870520	EP 1986-308545	19861103 <--
EP 222576	A3	19880323		
EP 222576	B1	19920318		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 4723010	A	19880202	US 1985-796359	19851107 <--
CA 1299178	C	19920421	CA 1986-520609	19861016 <--
AT 73801	T	19920415	AT 1986-308545	19861103 <--
IL 80475	A	19930131	IL 1986-80475	19861103 <--
ES 2032749	T3	19930301	ES 1986-308545	19861103 <--
CA 1293726	C	19911231	CA 1986-522156	19861104 <--
DK 8605298	A	19870508	DK 1986-5298	19861106 <--
DK 172010	B1	19970915		
FI 8604512	A	19870508	FI 1986-4512	19861106 <--
FI 87355	B	19920915		

FI 87355	C	19921228			
AU 8664858	A	19870611	AU 1986-64858		19861106 <--
AU 574589	B2	19880707			
CN 86108308	A	19870715	CN 1986-108308		19861106 <--
CN 1009831	B	19901003			
DD 254001	A5	19880210	DD 1986-296012		19861106 <--
ZA 8608450	A	19880629	ZA 1986-8450		19861106 <--
HU 46318	A2	19881028	HU 1986-4621		19861106 <--
HU 206338	B	19921028			
SU 1551246	A3	19900315	SU 1986-4028554		19861106 <--
NO 168303	B	19911028	NO 1986-4425		19861106 <--
NO 168303	C	19920205			
JP 62114988	A	19870526	JP 1986-265436		19861107 <--
JP 04001747	B	19920114			
PL 151024	B1	19900731	PL 1986-262266		19861107 <--
US 4748280	A	19880531	US 1987-79869		19870731 <--
CA 1290768	C2	19911015	CA 1990-615750		19900528 <--
PRIORITY APPLN. INFO.:			US 1985-796039	A	19851107 <--
			US 1985-796359	A	19851107 <--
			EP 1986-308545	A	19861103 <--
			CA 1986-522156	A	19861104 <--

OTHER SOURCE(S): CASREACT 107:176055; MARPAT 107:176055

ED Entered STN: 14 Nov 1987

AB The title compds. [I; R1 = OH, 'prodrug' group; R2 = (substituted) (benzo-fused) N-containing 5- or 6-membered heterocyclyl; R3, R4 = H, F, Cl, Br, CF3, alkyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, NO2; R3R4 = alkanedioxy; R5 = H, Me; X = O, S; Z = bond, O, S, NH, CH2] were prepared as aldose reductase inhibitors for treatment of diabetes-associated disorders (no data). Et 4-oxo-3H-phthalazine-1-ylacetate 11.5 g, NaH, and 5-bromo-2-(bromomethyl)**benzothiazole** 16.8 g were stirred in DMF for 1 h at room temperature to give 15.6 g I (R1 = OEt, R2 = 5- **bromobenzothiazol**-2-yl, R3 = R4 = R5 = H, X = Z = O) which (15.0 g) was saponified with KOH in dioxane to give 7.65 g I (R1 = OH).

IC ICM C07D417-06
ICS C07D413-14; C07D413-06; C07D403-06; C07D498-04; C07D417-12; C07D409-06; C07D513-04; A61K031-50

CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST **benzothiazolylmethylphthalazinylacetate** prepn aldose reductase inhibitor; cataract treatment **benzothiazolylmethylphthalazinylacetate**; retinopathy treatment **benzothiazolylmethylphthalazinylacetate*** ; **neuropathy treatment** ***benzothiazolylmethylphthalazineacetate**; phthalazinylacetate heterocyclyl diabetes treatment; oxadiazolylmethylphthalazinylacetate prepn aldose reductase inhibitor

IT 25947-14-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of, by (bromomethyl)**benzothiazole**)

IT 25947-13-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of, by (bromomethyl)**benzothiazole**, in preparation of aldose reductase inhibitors)

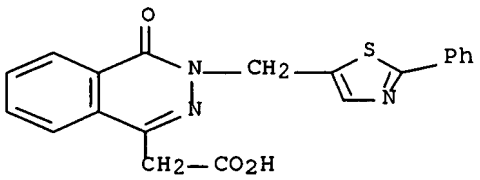
IT 137-07-5, 2-**Aminothiophenol** 4274-38-8 16867-03-1, 2-Amino-3-hydroxypyridine 38240-21-0, 3-Amino-2-mercaptopyridine 79811-34-0D, tin complex
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with chlorotriethoxyethane)

IT 110704-51-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, **benzothiazole** derivative by)

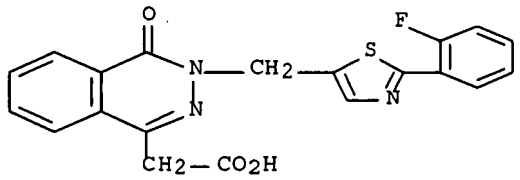
IT 110703-53-2P 110703-54-3P 110703-55-4P 110703-56-5P 110703-57-6P
110703-58-7P 110703-59-8P 110703-60-1P 110703-61-2P 110703-62-3P
110703-63-4P 110703-64-5P 110703-65-6P 110703-66-7P 110703-67-8P
110703-68-9P 110703-69-0P 110703-70-3P 110703-71-4P 110703-72-5P
110703-73-6P 110703-74-7P **110703-75-8P** **110703-76-9P**
110703-77-0P **110703-78-1P** 110703-79-2P 110703-80-5P
110703-81-6P 110703-82-7P 110703-83-8P 110703-84-9P 110703-85-0P
110703-86-1P 110703-87-2P 110703-88-3P **110703-89-4P**
110703-90-7P 110703-91-8P **110703-92-9P** 110703-93-0P
110703-94-1P 110703-95-2P 110703-96-3P 110703-97-4P 110703-98-5P
110703-99-6P 110704-00-2P 110704-01-3P 110704-02-4P 110704-53-5P
110704-61-5P 110721-48-7P 110721-49-8P 110721-50-1P 110721-51-2P
110721-52-3P 110721-53-4P 110721-54-5P 110721-55-6P 110721-56-7P
110721-57-8P 110721-58-9P 110721-59-0P 110721-60-3P 110721-61-4P
110721-62-5P 110721-63-6P 110721-64-7P 110721-65-8P 110721-66-9P
110721-67-0P 110721-68-1P 110721-69-2P 110721-70-5P 110721-71-6P
110721-72-7P 110721-73-8P 110721-74-9P 110721-75-0P 110721-76-1P
110721-77-2P 110721-78-3P 110721-79-4P 110721-80-7P 110721-81-8P
110721-82-9P 110721-83-0P 110721-84-1P 110721-85-2P 110721-86-3P
110721-87-4P 110721-88-5P 110721-89-6P 110721-90-9P 110721-91-0P
110721-92-1P 110721-93-2P 110721-94-3P 110722-32-2P 110722-33-3P
110722-34-4P 110722-35-5P 110722-36-6P 110722-37-7P 110722-38-8P
110722-39-9P 110722-40-2P 110722-41-3P 110722-42-4P 110722-43-5P
110722-44-6P 110722-45-7P 110722-46-8P 110749-07-0P 110749-08-1P
110749-09-2P 110765-49-6P 112065-65-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as aldose reductase inhibitor for treatment of diabetes-associated diseases)

IT **110703-75-8P** **110703-76-9P** **110703-78-1P**
110703-89-4P **110703-90-7P** **110703-92-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as aldose reductase inhibitor for treatment of diabetes-associated diseases)

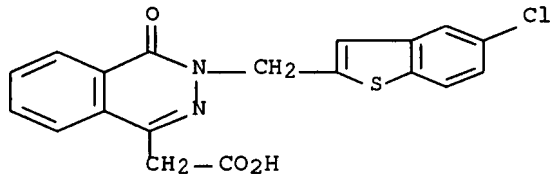
RN 110703-75-8 HCAPLUS
CN 1-Phthalazineacetic acid, 3,4-dihydro-4-oxo-3-[(2-phenyl-5-thiazolyl)methyl]- (9CI) (CA INDEX NAME)



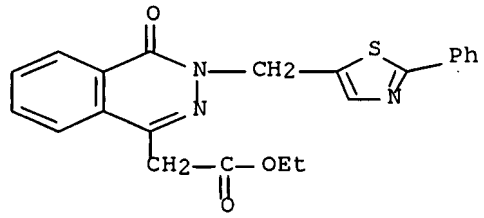
RN 110703-76-9 HCAPLUS
CN 1-Phthalazineacetic acid, 3-[[2-(2-fluorophenyl)-5-thiazolyl]methyl]-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



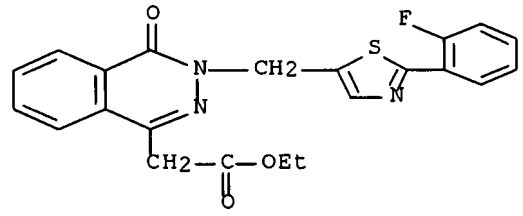
RN 110703-78-1 HCAPLUS
CN 1-Phthalazineacetic acid, 3-[(5-chlorobenzo[b]thien-2-yl)methyl]-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



RN 110703-89-4 HCAPLUS
CN 1-Phthalazineacetic acid, 3,4-dihydro-4-oxo-3-[(2-phenyl-5-thiazolyl)methyl]-, ethyl ester (9CI) (CA INDEX NAME)

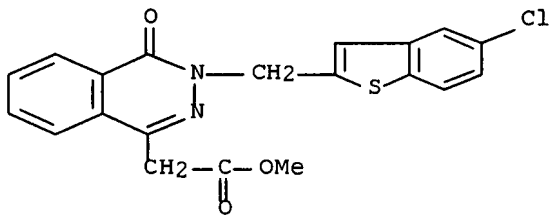


RN 110703-90-7 HCAPLUS
CN 1-Phthalazineacetic acid, 3-[[2-(2-fluorophenyl)-5-thiazolyl]methyl]-3,4-dihydro-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



RN 110703-92-9 HCAPLUS

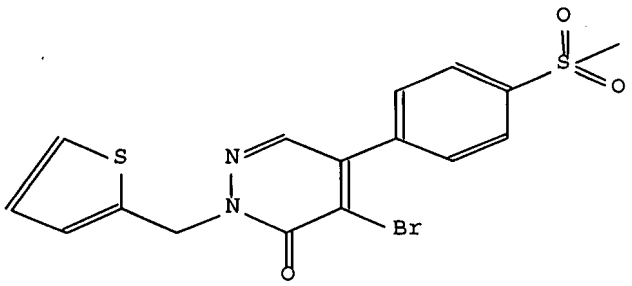
CN 1-Phthalazineacetic acid, 3-[(5-chlorobenzo[b]thien-2-yl)methyl]-3,4-dihydro-4-oxo-, methyl ester (9CI) (CA INDEX NAME)



=> d l50 ide
YOU HAVE REQUESTED DATA FROM FILE 'BEILSTEIN' - CONTINUE? (Y)/N:y

L50 ANSWER 1 OF 1 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

Beilstein Records (BRN):	9344517
Chemical Name (CN):	4-bromo-5-(4-methanesulfonyl-phenyl)-2-thiophen-2-ylmethyl-2H-pyridazin-3-one
Autonom Name (AUN):	4-bromo-5-(4-methanesulfonyl-phenyl)-2-thiophen-2-ylmethyl-2H-pyridazin-3-one
Molec. Formula (MF):	C16 H13 Br N2 O3 S2
Molecular Weight (MW):	425.31
Lawson Number (LN):	29066, 20730, 292
Compound Type (CTYPE):	heterocyclic
Constitution ID (CONSID):	7888607
Tautomer ID (TAUTID):	8768875
Entry Date (DED):	2003/07/25
Update Date (DUPD):	2003/07/25



Field Availability:

Code	Name	Occurrence

BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	3
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
DED	Entry Date	1
DUPD	Update Date	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	2
RXREA	Substance is Reaction Reactant	1
RXPRO	Substance is Reaction Product	1

```
=> d l50 rx
YOU HAVE REQUESTED DATA FROM FILE 'BEILSTEIN' - CONTINUE? (Y)/N:y



L50  ANSWER 1 OF 1 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

Reaction:
RX
     Reaction ID (.ID):              9250928
     Reactant BRN (.RBRN):           9332509
     Reactant (.RCT):                4-bromo-5-(4-methanesulfonyl-phenyl)-2H-
                                     pyridazin-3-one, 2-thienylmethyl halide
     Product BRN (.PBRN):            9344517
     Product (.PRO):                 4-bromo-5-(4-methanesulfonyl-phenyl)-2-
                                     thiophen-2-ylmethyl-2H-pyridazin-3-one
     No. of React. Details (.NVAR):  1

Reaction Details:
RX
     Reaction RID (.RID):            9250928.1
     Reaction Classification (.CL):  Preparation
     Reagent (.RGT):                 base
     Reference(s):
     1. Li, Chun Sing; Brideau, Christine; Chan, Chi Chung; Savoie, Chantal;
        Claveau, David; Charleson, Stella; Gordon, Robert; Greig, Gillian;
        Gauthier, Jacques Yves; Lau, Cheuk K.; Riendeau, Denis; et al.,
        Bioorg.Med.Chem.Lett., CODEN: BMCLE8, 13(4), <2003>, 597 - 600;
        BABS-6388164

Reaction:
RX
     Reaction ID (.ID):              9250533
     Reactant BRN (.RBRN):           9344517, 2829653
     Reactant (.RCT):                4-bromo-5-(4-methanesulfonyl-phenyl)-2-
                                     thiophen-2-ylmethyl-2H-pyridazin-3-one,
                                     (4-fluoro-phenyl)-dihydroxy-borane
```

Product BRN (.PBRN): 9353562
Product (.PRO): 4-(4-fluoro-phenyl)-5-(4-methanesulfonyl-phenyl)-2-thiophen-2-ylmethyl-2H-pyridazin-3-one
No. of React. Details (.NVAR): 1

Reaction Details:
RX
Reaction RID (.RID): 9250533.1
Reaction Classification (.CL): Preparation
Catalyst (.CAT): Pd(0)
Reaction Type (.TYP): Suzuki coupling
Reference(s):
1. Li, Chun Sing; Brideau, Christine; Chan, Chi Chung; Savoie, Chantal; Claveau, David; Charleson, Stella; Gordon, Robert; Greig, Gillian; Gauthier, Jacques Yves; Lau, Cheuk K.; Riendeau, Denis; et al., Bioorg.Med.Chem.Lett., CODEN: BMCLE8, 13(4), <2003>, 597 - 600; BABS-6388164

=> d ibib ab hitstr 33-34
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX, WPIX, MEDLINE, EMBASE, DRUGU, MARPAT' - CONTINUE? (Y)/N:y

L99 ANSWER 33 OF 69 USPATFULL on STN
ACCESSION NUMBER: 2005:255662 USPATFULL Full-text
TITLE: Thiazole derivatives as **phosphodiesterase** iv inhibitors
INVENTOR(S): Eggenweiler, Hans-Michael, Darmstadt, GERMANY, FEDERAL REPUBLIC OF
Wolf, Michael, Darmstadt, GERMANY, FEDERAL REPUBLIC OF

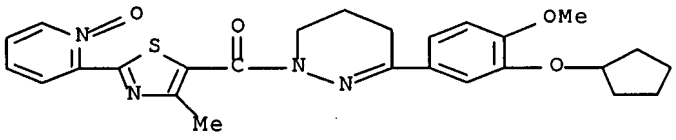
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005222160	A1	20051006	
APPLICATION INFO.:	US 2003-518503	A1	20030428	(10)
	WO 2003-EP4434		20030428	
			20041220	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	DE 2002-10227269	20020619

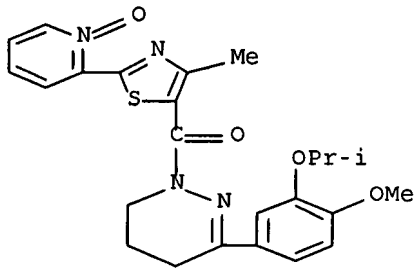
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201, US
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
LINE COUNT: 3103
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Thiazole derivatives of the formula I ##STR1## in which R.sup.1, R.sup.2, R.sup.3, V, W, X and B are as defined in claim 1, act as **phosphodiesterase** IV inhibitors and can be employed for the treatment of osteoporosis, tumours, cachexia, atherosclerosis, rheumatoid arthritis, multiple sclerosis, diabetes mellitus, inflammatory processes, allergies, asthma, autoimmune diseases, myocardial diseases and AIDS.
IT **640743-35-7P** **640743-36-8P** **640743-37-9P**
640743-38-0P, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-

pyridazin-1-yl]-1-(4-methyl-2-pyridin-3-ylthiazol-5-yl)methanone
640743-39-1P, 1-[3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyridin-3-ylthiazol-5-yl)methanone
640743-40-4P, 1-[3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyridin-3-ylthiazol-5-yl)methanone
640743-41-5P, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyridin-2-ylthiazol-5-yl)methanone
640743-42-6P, 1-[3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyridin-2-ylthiazol-5-yl)methanone
640743-43-7P, 1-[3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyridin-2-ylthiazol-5-yl)methanone
640743-44-8P, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyrazin-2-ylthiazol-5-yl)methanone
640743-45-9P, 1-[3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyrazin-2-ylthiazol-5-yl)methanone
640743-46-0P, 1-[3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-pyrazin-2-ylthiazol-5-yl)methanone
640743-47-1P, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-thiophen-2-ylthiazol-5-yl)methanone
640743-48-2P, 1-[3-(3-Isopropoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-thiophen-2-ylthiazol-5-yl)methanone
640743-49-3P, 1-[3-(3-Cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-thiophen-2-ylthiazol-5-yl)methanone
640743-50-6P, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-(4-methyl-2-phenylthiazol-5-yl)methanone
640743-51-7P, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-[4-methyl-2-(4-methoxyphenyl)thiazol-5-yl]methanone
640743-52-8P, 1-[3-(3-Ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-1-[4-methyl-2-(4-aminophenyl)thiazol-5-yl]methanone
640743-53-9P **640743-54-0P**
(drug candidate; preparation of thiazoles as **phosphodiesterase** IV inhibitors for the treatment of osteoporosis, tumors and cachexia)

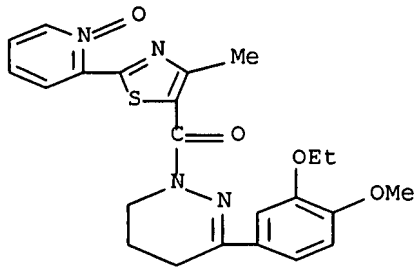
RN 640743-35-7 USPATFULL
CN Pyridazine, 3-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,4,5,6-tetrahydro-1-[[4-methyl-2-(1-oxido-2-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



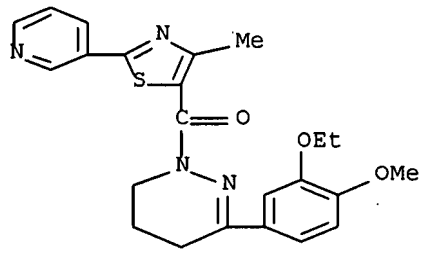
RN 640743-36-8 USPATFULL
CN Pyridazine, 1,4,5,6-tetrahydro-3-[4-methoxy-3-(1-methylethoxy)phenyl]-1-[[4-methyl-2-(1-oxido-2-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



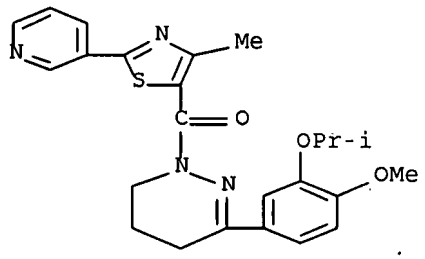
RN 640743-37-9 USPATFULL
CN Pyridazine, 3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro-1-[[4-methyl-2-(1-oxido-2-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



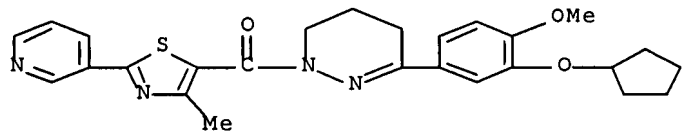
RN 640743-38-0 USPATFULL
CN Pyridazine, 3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro-1-[[4-methyl-2-(3-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



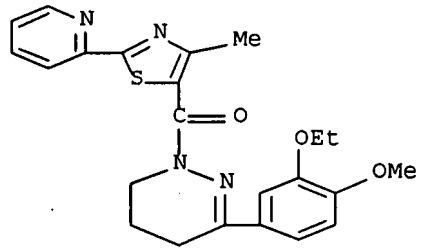
RN 640743-39-1 USPATFULL
CN Pyridazine, 1,4,5,6-tetrahydro-3-[4-methoxy-3-(1-methylethoxy)phenyl]-1-[[4-methyl-2-(3-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



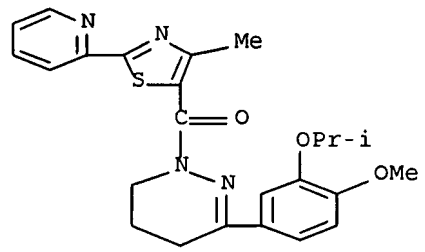
RN 640743-40-4 USPATFULL
CN Pyridazine, 3-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,4,5,6-tetrahydro-1-[[4-methyl-2-(3-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



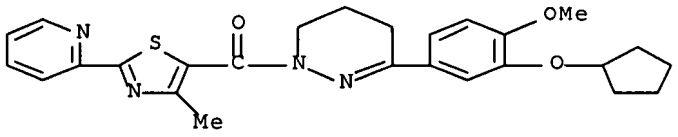
RN 640743-41-5 USPATFULL
CN Pyridazine, 3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro-1-[[4-methyl-2-(2-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



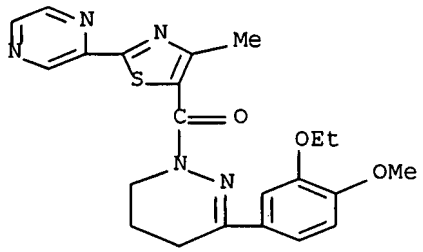
RN 640743-42-6 USPATFULL
CN Pyridazine, 1,4,5,6-tetrahydro-3-[4-methoxy-3-(1-methylethoxy)phenyl]-1-[[4-methyl-2-(2-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



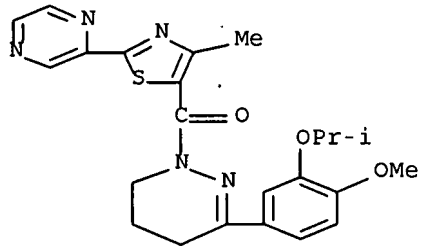
RN 640743-43-7 USPATFULL
CN Pyridazine, 3-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,4,5,6-tetrahydro-1-[[4-methyl-2-(2-pyridinyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



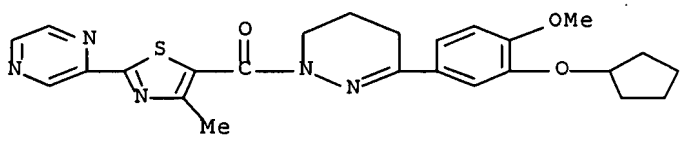
RN 640743-44-8 USPATFULL
CN Pyridazine, 3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro-1-[(4-methyl-2-pyrazinyl-5-thiazolyl)carbonyl]- (9CI) (CA INDEX NAME)



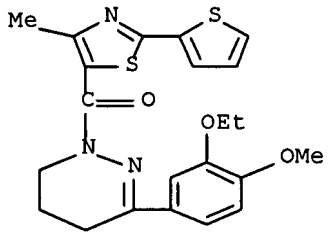
RN 640743-45-9 USPATFULL
CN Pyridazine, 1,4,5,6-tetrahydro-3-[4-methoxy-3-(1-methylethoxy)phenyl]-1-[(4-methyl-2-pyrazinyl-5-thiazolyl)carbonyl]- (9CI) (CA INDEX NAME)



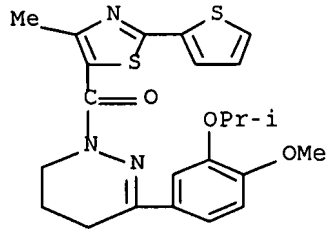
RN 640743-46-0 USPATFULL
CN Pyridazine, 3-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,4,5,6-tetrahydro-1-[(4-methyl-2-pyrazinyl-5-thiazolyl)carbonyl]- (9CI) (CA INDEX NAME)



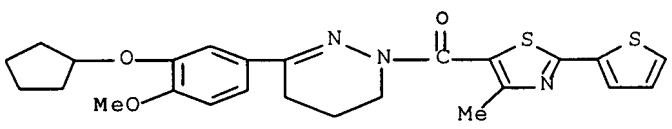
RN 640743-47-1 USPATFULL
CN Pyridazine, 3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro-1-[[4-methyl-2-(2-thienyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



RN 640743-48-2 USPATFULL
CN Pyridazine, 1,4,5,6-tetrahydro-3-[4-methoxy-3-(1-methylethoxy)phenyl]-1-[[4-methyl-2-(2-thienyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)

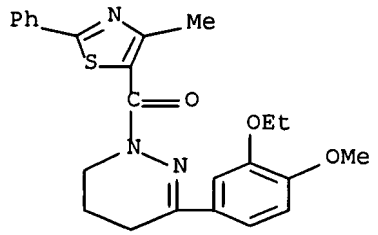


RN 640743-49-3 USPATFULL
CN Pyridazine, 3-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,4,5,6-tetrahydro-1-[[4-methyl-2-(2-thienyl)-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)

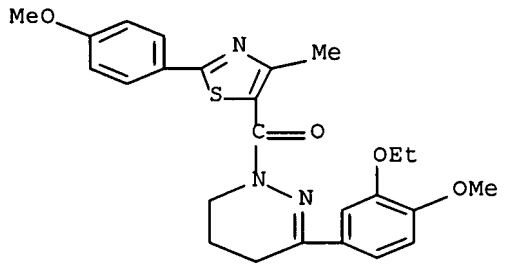


RN 640743-50-6 USPATFULL
CN Pyridazine, 3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro-1-[(4-methyl-2-

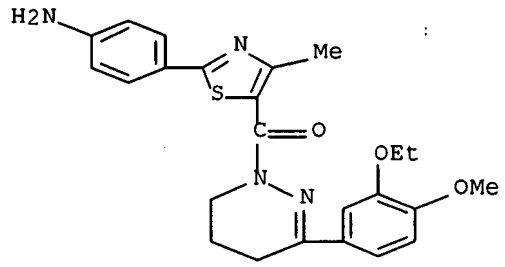
phenyl-5-thiazolyl)carbonyl]- (9CI) (CA INDEX NAME)



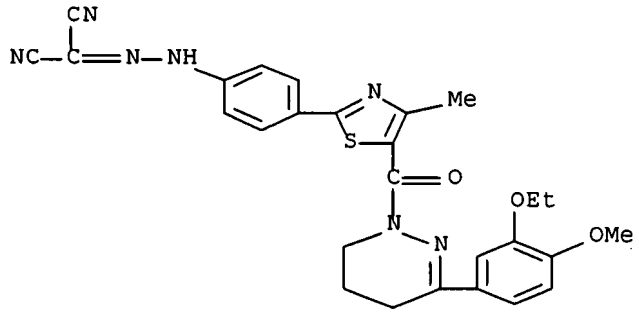
RN 640743-51-7 USPATFULL
CN Pyridazine, 3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro-1-[[2-(4-methoxyphenyl)-4-methyl-5-thiazolyl]carbonyl]- (9CI) (CA INDEX NAME)



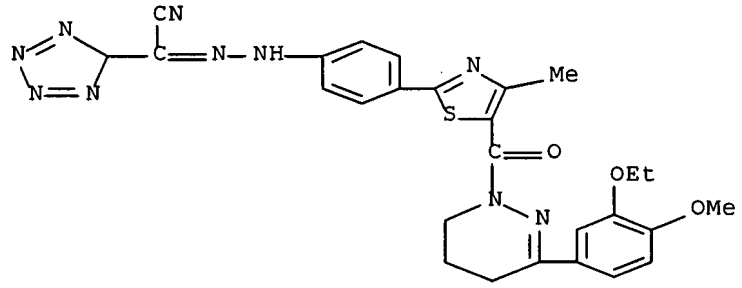
RN 640743-52-8 USPATFULL
CN Pyridazine, 1-[[2-(4-aminophenyl)-4-methyl-5-thiazolyl]carbonyl]-3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro- (9CI) (CA INDEX NAME)



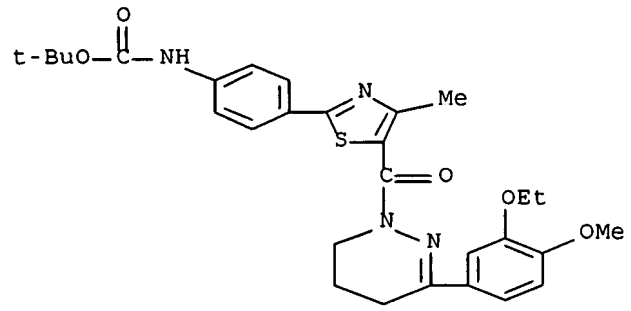
RN 640743-53-9 USPATFULL
CN Pyridazine, 1-[[2-[4-[(dicyanomethylene)hydrazino]phenyl]-4-methyl-5-thiazolyl]carbonyl]-3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro- (9CI) (CA INDEX NAME)



RN 640743-54-0 USPATFULL
CN Pyridazine, 1-[[2-[4-[(cyano-5H-tetrazol-5-ylmethylene)hydrazino]phenyl]-4-methyl-5-thiazolyl]carbonyl]-3-(3-ethoxy-4-methoxyphenyl)-1,4,5,6-tetrahydro- (9CI) (CA INDEX NAME)



IT **640743-64-2**
(preparation of thiazoles as **phosphodiesterase** IV inhibitors for the treatment of osteoporosis, tumors and cachexia)
RN 640743-64-2 USPATFULL
CN Carbamic acid, [4-[5-[[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-1(4H)-pyridazinyl]carbonyl]-4-methyl-2-thiazolyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L99 ANSWER 34 OF 69 USPATFULL on STN

ACCESSION NUMBER: 2001:173588 USPATFULL Full-text
TITLE: Thieno[2,3-d]pyrimidine-2,4-diones
INVENTOR(S): Bantick, John, Burton-on-the-Wolds, United Kingdom
Cooper, Martin, Loughborough, United Kingdom
Perry, Matthew, Loughborough, United Kingdom
Thorne, Philip, Loughborough, United Kingdom
PATENT ASSIGNEE(S): AstraZeneca AB, Sodertalje, Sweden (non-U.S. corporation)

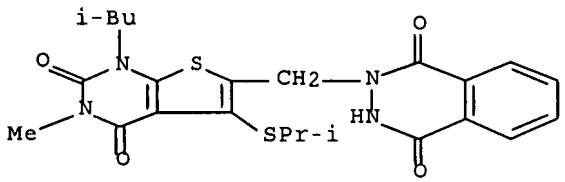
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6300334	B1	20011009	
	WO 2000012514		20000309	
APPLICATION INFO.:	US 1999-402837		19991013	(9)
	WO 1999-SE1400		19990818	
			19991013	PCT 371 date
			19991013	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	SE 1998-2895	19980828

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Shah, Mukund J.
ASSISTANT EXAMINER: McKenzie, Thoams C.
LEGAL REPRESENTATIVE: Nixon & Vanderhye
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 2510
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of formula (I): ##STR1##

wherein R.sup.1, R.sup.2, and R.sup.3 are defined in the specification. The compounds are useful for treating or reducing the risk of reversible obstructive airways disease.

IT **259861-99-9P**
(target compound; preparation of thieno[2,3-d]pyrimidine-2,4(1H,3H)-diones as immunosuppressants)
RN 259861-99-9 USPATFULL
CN 1,4-Phthalazinedione, 2,3-dihydro-2-[[1,2,3,4-tetrahydro-3-methyl-5-[(1-methylethyl)thio]-1-(2-methylpropyl)-2,4-dioxothieno[2,3-d]pyrimidin-6-yl]methyl]- (9CI) (CA INDEX NAME)



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YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX, WPIX, MEDLINE, EMBASE, DRUGU, MARPAT' - CONTINUE? (Y)/N:y

L99 ANSWER 35 OF 69 TOXCENTER COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:125146 TOXCENTER Full-text
COPYRIGHT: Copyright 2006 ACS
DOCUMENT NUMBER: CA12413176127Q
TITLE: Preparation of sulfamoylindanyl- and sulfamoyl-1,2,3,4-tetrahydronaphthylpyridazinone derivatives as drugs
AUTHOR(S): Ishida, Akihiko; Pponma, Koichi; Kono, Haruyuki; Tamura, Koji; Sasaki, Yasuhiko
CORPORATE SOURCE: ASSIGNEE: Tanabe Seiyaku Co
PATENT INFORMATION: JP 95233072 A2 5 Sep 1995
SOURCE: (1995) Jpn. Kokai Tokkyo Koho, 35 pp.
CODEN: JKXXAF.
COUNTRY: JAPAN
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1996:52662
LANGUAGE: Japanese
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 27 May 2003
ED Entered STN: 16 Nov 2001
Last Updated on STN: 27 May 2003
AB The title compds. [I; R1 = (un)substituted C1-10 alkyl, C3-6 cycloalkyl, lower alkenyl, (un)substituted heterocyclyl containing N, O, or S heteroatom, camphor-10-yl; R3 = H, (un)substituted lower alkyl, lower alkenyl; or R1 and R3 are linked to each other at the termini to form a lower alkylene; R2 = H, (un)substituted lower alkyl, aryl, lower alkenyl; A-B = ethylene or vinylene optionally substituted by 1-2 groups selected from lower alkyl or Ph; n = 1,2; D = H, halo], which are useful for the treatment and prevention of nephritis, in particular glomerulonephritis, IgA nephritis, nephrotic syndrome, and/or lupus nephritis and as blood platelet aggregation inhibitors and/or protective agents against endotoxin shock, are prepared Thus, 1.15 g 2-amino-5-[3-oxo-3(H)-4,5-dihydropyridazin-6- yl]indan was dissolved in EtOAc and THF, followed by successively adding an aqueous solution of 1.4 g K2CO3 in 20 mL and 0.57 g MeSO2Cl, and the resulting mixture was stirred for 2 h to give 1.08 g 2-methanesulfonylamino-5-[3-oxo- 3(H)-4,5-dihydropyridazin-6-yl]indan (II). Mice was administered with II at 100 mg/kg p.o. and after 30 min treated with a solution of Escherichia coli-derived endotoxin (lipopolysaccharides) in physiol. saline at 100 mg/10 mL/kg i.p. The survival ratio of the treated mice was 100 %.
CC 28-15
ST Miscellaneous Descriptors
sulfamoylindanylpyridazinone prepn treatment nephritis; sulfamoyltetrahydronaphthylpyridazinone prepn treatment nephrotic syndrome; glomerulonephritis treatment sulfamoylindanylpyridazinone; IgA nephritis treatment sulfamoylindanylpyridazinone; lupus nephritis treatment sulfamoylindanylpyridazinone; blood platelet aggregation inhibitor sulfamoylindanylpyridazinone; endotoxin shock protection sulfamoylindanylpyridazinone; indanylpyridazinone sulfamoyl prepn treatment nephritis; naphthylpyridazinone sulfamoyl prepn treatment nephrotic syndrome; pyridazinone sulfamoyl indanyl prepn treatment nephritis
RN 74-88-4 (Methyl iodide)
75-36-5 (Acetyl chloride)
75-86-5 (Acetone cyanohydrin)
79-30-1 (2-Methylpropanoyl chloride)

85-44-9 (Phthalic anhydride)
96-32-2 (Methyl bromoacetate)
100-39-0 (Benzyl bromide)
100-52-7 (Benzaldehyde)
103-80-0 (Phenylacetyl chloride)
105-36-2 (Ethyl bromoacetate)
106-65-0 (Dimethyl succinate)
107-08-4 (Propyl iodide)
107-99-3 (2-Dimethylaminoethyl chloride)
108-30-5 (Succinic anhydride)
108-90-7 (Chlorobenzene)
123-38-6 (Propanal)
124-63-0 (Methanesulfonyl chloride)
677-25-8 (Vinylsulfonyl fluoride)
1490-25-1 (Methyl succinyl chloride)
1622-32-8 (2-Chloroethanesulfonyl chloride)
1633-82-5 (3-Chloropropanesulfonyl chloride)
2386-60-9 (n-Butanesulfonyl chloride)
2975-41-9 (2-Aminoindan)
3099-31-8 (3-Picolyl chloride)
3144-16-9 ((+)-Camphorsulfonic acid)
3878-55-5 (Methyl hydrogen succinate)
7803-57-8 (Hydrazine hydrate)
10147-36-1 (Propanesulfonyl chloride)
16629-19-9 (2-Thiophenesulfonyl chloride)
79686-90-1 (2-Methoxycarbonylaminosuccinic anhydride)
138006-38-9 (2-Propionylaminoindan)
64624-93-7 (2-Propylindan)
155719-25-8 (2-Butanesulfonylaminoindan)

RN 155718-08-4; 155718-25-5; 155718-33-5; 155718-34-6; 155718-80-2;
155719-82-7; 172679-62-8; 172679-63-9; 172679-64-0; 172679-65-1;
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YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX, WPIX, MEDLINE, EMBASE, DRUGU, MARPAT' - CONTINUE? (Y)/N:y

'IBIB' IS NOT A VALID FORMAT
'ED' IS NOT A VALID FORMAT
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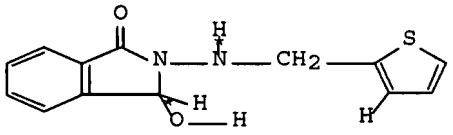
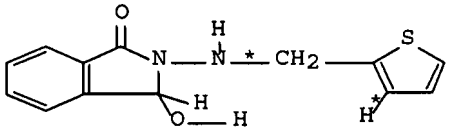
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):bib ab hit

L99 ANSWER 36 OF 69 CHEMINFORMRX COPYRIGHT 2006 FIZ CHEMIE on STN
AN 200409129 CHEMINFORMRX Full-text
TI Regioselective Reduction of 2-(Arylideneamino)isoindole-1,3-diones - Synthesis of Alkaloid Analogues by N-Acylhydrazonium Ion Aromatic π-Cyclization.
AU FOGAIN-NINKAM, A.; DAICH, A.; DECROIX, B.; NETCHITAILO, P.
CS URCOM, Univ. Le Havre, F-76058 Le Havre, Fr.
SO Eur. J. Org. Chem.(21), 4273-4278 (2003)
CODEN: EJOCFK ISSN: 1434-193X
LA English
AB In the presence of NaBH3CN, 2-(arylideneamino)isoindole-1,3-diones undergo regioselective reduction yielding hydrazines like (IV) and (IX). Subsequent reaction with methanolic NaBH4 at 5°C results in regioselective formation of hydroxylactams such as (V) and (XII). Treatment of the latter or their acetoxy derivatives with acids leads to N-acylhydrazonium ions which smoothly undergo cyclization to fused pyridazines. Unexpectedly, starting from the hydroxylactams (Vb) and (Vc) thienylmethyl-substituted derivatives such as (IX) are obtained.

RX(12) OF 59 ...2 S ===> AA

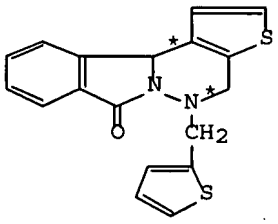


V



V

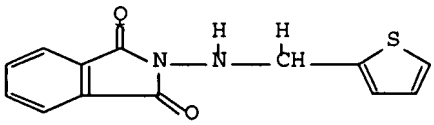
(12) →



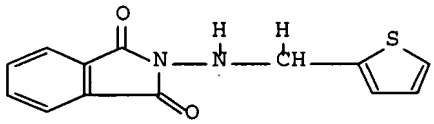
IX
YIELD 41.0%

RX(12) RCT V, 996734
RGT 219 (76-05-1), TFA
PRO IX, **996738**
YDS 41.0 %
T 25.0 Cel
KW arylation; alkylation; C-alkylation
NTE reaction:Vb -> IX

RX(32) OF 59 COMPOSED OF RX(8), RX(12)
RX(32) 2 O ===> AA

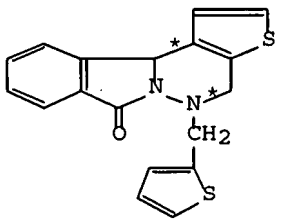


IV



IV

2 STEPS →

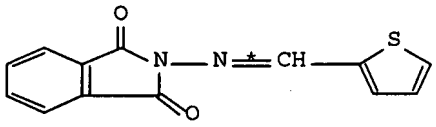


IX
YIELD 41.0%

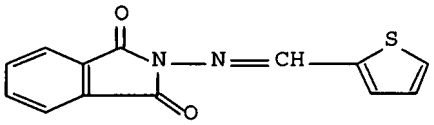
RX(8) RCT IV, 996731
RGT 1156 (16940-66-2), NaBH4
SOL 123 (67-56-1), MeOH
PRO V, 996734
YDS 71.0 %
T 5.0 Cel
KW addition; hydrogenation
NTE reaction:IV -> V, example: 2
RX(12) RCT V, 996734
RGT 219 (76-05-1), TFA
PRO IX, **996738**

YDS 41.0 %
T 25.0 Cel
KW arylation; alkylation; C-alkylation
NTE reaction:Vb -> IX

RX(48) OF 59 COMPOSED OF RX(5), RX(8), RX(12)
RX(48) 2 F ===> AA

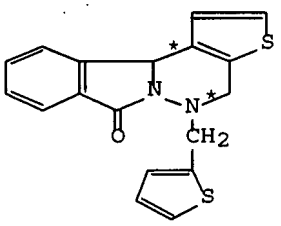


III



III

3 STEPS



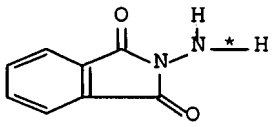
IX
YIELD 41.0%

RX(5) RCT III, 996729
RGT 430 (25895-60-7), NaBH3CN
103 (7647-01-0), HCl
SOL 123 (67-56-1), MeOH
PRO IV, 996731
YDS 74.0 %
T 10.0 - 25.0 Cel
KW addition; hydrogenation
NTE reaction:III -> IV, example: 2

RX(8) RCT IV, 996731
RGT 1156 (16940-66-2), NaBH4
SOL 123 (67-56-1), MeOH
PRO V, 996734
YDS 71.0 %
T 5.0 Cel
KW addition; hydrogenation
NTE reaction:IV -> V, example: 2

RX(12) RCT V, 996734
RGT 219 (76-05-1), TFA
PRO IX, **996738**
YDS 41.0 %
T 25.0 Cel
KW arylation; alkylation; C-alkylation
NTE reaction:Vb -> IX

RX(49) OF 59 COMPOSED OF RX(2), RX(5), RX(8), RX(12)
RX(49) 2 A + 2 E ===> AA



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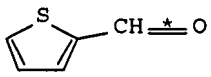

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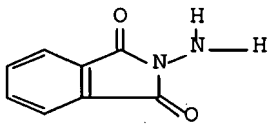

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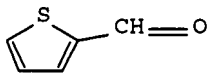
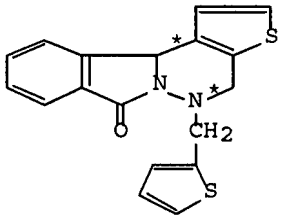


II

4
STEPS



IX
YIELD 41.0%

RX(2) RCT I, 12345 (1875-48-5)
II, 12824 (98-03-3)
SOL 214 (108-88-3), toluene
CAT 517 (104-15-4), TosOH
PRO III, 996729
YDS 83.0 %
T.KW REFLUX
NTE reaction:I (II) -> III, example: 2

RX(5) RCT III, 996729
RGT 430 (25895-60-7), NaBH3CN
103 (7647-01-0), HCl
SOL 123 (67-56-1), MeOH
PRO IV, 996731
YDS 74.0 %
T 10.0 - 25.0 Cel
KW addition; hydrogenation
NTE reaction:III -> IV, example: 2

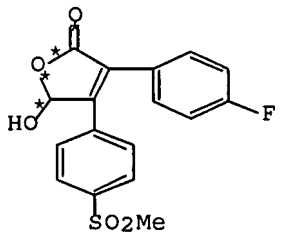
RX(8) RCT IV, 996731
RGT 1156 (16940-66-2), NaBH4
SOL 123 (67-56-1), MeOH
PRO V, 996734
YDS 71.0 %
T 5.0 Cel
KW addition; hydrogenation
NTE reaction:IV -> V, example: 2

RX(12) RCT V, 996734
RGT 219 (76-05-1), TFA
PRO IX, **996738**
YDS 41.0 %
T 25.0 Cel
KW arylation; alkylation; C-alkylation
NTE reaction:Vb -> IX

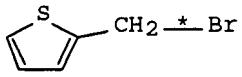
=> d bib ab hit 37
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX, WPIX, MEDLINE, EMBASE, DRUGU, MARPAT' - CONTINUE? (Y)/N:y

L99 ANSWER 37 OF 69 CHEMINFORMRX COPYRIGHT 2006 FIZ CHEMIE on STN
AN 200325164 CHEMINFORMRX Full-text
TI Pyridazinones as Selective Cyclooxygenase-2 Inhibitors.
AU LI, C. S.; ET AL.
CS Merck Frosst Cent. Ther. Res., Pointe-Claire-Dorval, Que. H9R 4P8, Can.
SO Bioorg. Med. Chem. Lett., 13(4), 597-600 (2003)
CODEN: BMCLE8 ISSN: 0960-894X
LA English
AB The preparation of title compounds such as (VI) and (XIII) following simple reaction pathways and evaluation of their structure-activity relationship as a new class of orally active COX-2 inhibitors based on the six-membered heterocyclic pyridazinone system are reported. Two potent and selective COX-2 inhibitors (VI) and (XIII) are identified.

RX(5) OF 21 ...H + P ===> Q

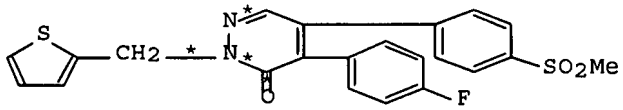


II



III

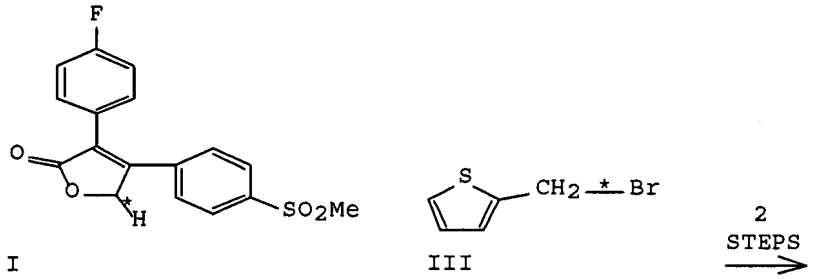
(5) →



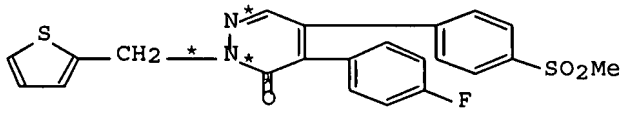
IV
YIELD 30.0-75.0%

RX(5) RCT II, 953532
III, 151272 (45438-73-1)
STAGE(1)
RGT 582 (302-01-2), H2N-NH2
STAGE(2)
RGT 1159 (1310-73-2), NaOH
SOL 76 (68-12-2), DMF
PRO IV, **953535**
YDS 30.0 - 75.0 %
KW acylation; N-acylation; alkylation; N-alkylation
NTE reaction:II 2.(III) -> IV, example: 3

RX(14) OF 21 COMPOSED OF RX(2), RX(5)
RX(14) G + P ===> Q



I III



IV
YIELD 30.0-75.0%

RX(2) RCT I, 953531
STAGE(1)
RGT 1135 (128-08-5), NBS
STAGE(2)
RGT 3 (64-19-7), AcOH
SOL 206 (109-99-9), THF
222 (7732-18-5), H2O
PRO II, 953532
YDS 45.0 %
KW alkylation; O-alkylation
NTE reaction:I -> II, example: 2
RX(5) RCT II, 953532
III, 151272 (45438-73-1)
STAGE(1)
RGT 582 (302-01-2), H2N-NH2
STAGE(2)
RGT 1159 (1310-73-2), NaOH
SOL 76 (68-12-2), DMF
PRO IV, **953535**
YDS 30.0 - 75.0 %
KW acylation; N-acylation; alkylation; N-alkylation
NTE reaction:II 2.(III) -> IV, example: 3

=> d iall abeq tech abex hitstr 38-42
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX, WPIX, MEDLINE, EMBASE, DRUGU, MARPAT' - CONTINUE? (Y)/N:y

L99 ANSWER 38 OF 69 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-603388 [58] WPIX
CROSS REFERENCE: 1999-190573; 2000-350672; 2002-279861; 2002-361139; 2004-069781
DOC. NO. CPI: C2004-218616 [58]
TITLE: New pyridazinone compounds are cyclooxygenase-2 inhibitors used for treating e.g. rheumatoid arthritis, fever and inflammation
DERWENT CLASS: B02; B03
INVENTOR: BASHA A; BLACK L A; COGHLAN M J; KOLASA T; KORT M E; LIU H; MCCARTY C M; PATEL M; ROHDE J J; STEWART A O
PATENT ASSIGNEE: (BASH-I) BASHA A; (BLAC-I) BLACK L A; (COGH-I) COGHLAN M J; (KOLA-I) KOLASA T; (KORT-I) KORT M E; (LIUH-I) LIU H; (MCCA-I) MCCARTY C M; (PATE-I) PATEL M; (ROHD-I) ROHDE J J; (STEW-I) STEWART A O; (ABBO-C) ABBOTT LAB
COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20040158064	A1	20040812	(200458)*	EN	158[0]	
US 7115591	B2	20061003	(200665)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20040158064	A1 Provisional	US 1997-56733P	19970822
US 20040158064	A1 CIP of	US 1998-129570	19980805
US 20040158064	A1 CIP of	US 1998-179605	19981027
US 20040158064	A1 CIP of	US 1999-261872	19990303
US 20040158064	A1 Div Ex	US 1999-427768	19991027
US 20040158064	A1 Div Ex	US 2001-871195	20010531
US 20040158064	A1	US 2003-464928	20030619

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 20040158064	A1 Div ex	US 6307047 B

PRIORITY APPLN. INFO: US 2003-464928 20030619
US 1997-56733P 19970822
US 1998-129570 19980805
US 1998-179605 19981027
US 1999-261872 19990303
US 1999-427768 19991027
US 2001-871195 20010531
INT. PATENT CLASSIF.:
IPC ORIGINAL: A61K0031-50 [I,A]; A61K0031-675 [I,A]; C07D0237-00 [I,C]; C07D0237-16 [I,A]; C07F0009-00 [I,C]; C07F0009-6509 [I,A]
IPC RECLASSIF.: C07D0237-00 [I,C]; C07D0237-14 [I,A]; C07D0405-00 [I,C]; C07D0405-04 [I,A]; C07D0409-00 [I,C]; C07D0409-04 [I,A]

BASIC ABSTRACT:

US 20040158064 A1 UPAB: 20050531

NOVELTY - Pyridazinone compounds (I), are new.

DETAILED DESCRIPTION - Pyridazinone compounds of formula (I) and their salts, esters and prodrugs are new.

X = O, S, NR4, NORa or NNRbRc;

R4 = alkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, arylalkyl, cycloalkenylalkyl, cycloalkylalkyl, heterocyclyl or heterocyclylalkyl;

Ra-Rc = alkyl, cycloalkyl, aryl or arylalkyl;

R = alkyl, alkenyl, alkoxy, alkoxyalkyl, alkoxyhaloalkyl, alkoxyiminoalkoxy, alkylcarbonylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkoxy, arylalkyl, arylhaloalkyl, arylalkynyl, arylhydroxyalkyl, aryloxy, aryloxyhydroxyalkyl, arylcarbonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkylalkyl, cycloalkylidenealkyl, haloalkenyl, haloalkoxyhydroxyalkyl, haloalkyl, haloalkenyl, heterocyclyl, heterocyclylalkoxy, heterocyclylalkyl, heterocyclyloxy, hydroxyalkyl, hydroxyiminoalkyl, (CH2)nC(O)R5, (CH2)nCH(OH)R5, (CH2)nC(NORd)R5, (CH2)nCH(NORd)R5, (CH2)nCH(NRdRe)R5, R6R7, (CH2)nCCR7, (CH2)n(CH((CX')3)m(CH2)pR7, (CH2)n(C(C(X')2)m(CH2)pR7 or (CH2)n(CHX')m(CH2)pR7;

R5 = T, haloalkenyl or haloalkynyl;

T = H, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, arylalkyl, haloalkyl, heterocyclyl or heterocyclylalkyl;

R6 = alkenylene or alkylene (both optionally substituted by halo);

R7, Rd, Re = T;

X' = halo;

m = 0-5;

n, p = 0-10;

R1-R3 = H, alkenyl, cycloalkenyl, alkoxyalkyl, alkoxyiminoalkoxy, alkoxyiminoalkyl, alkyl, cycloalkyl, alkylcarbonylalkoxy, alkylcarbonylamino, alkylcarbonylaminoalkyl, alkynyl, aminoalkoxy, aminoalkylcarbonyloxyalkoxy, aminocarbonylalkyl, aryl, arylalkenyl, arylalkyl, arylalkynyl, carboxyalkylcarbonyloxyalkoxy, cyano, cycloalkylidenealkyl, haloalkenyloxy, haloalkoxy, haloalkyl, halo, heterocyclic, hydroxyalkoxy, hydroxyiminoalkoxy, hydroxyiminoalkyl, mercaptoalkoxy, nitro, phosphonatoalkoxy, Y or W;

W = a group of formula (i) or (ii);

X1 = S(O)2, S(O)(NR10), S(O), Se(O)2, P(O)(OR11) or P(O)(NR12R13);

X2 = H, alkenyl, cycloalkenyl, alkyl, cycloalkyl, alkynyl or halo;

R9 = alkenyl, alkoxy, alkyl, alkylamino, dialkylamino, alkylcarbonylamino, alkynyl, amino, NHNH2 or NCHN(R10R11);

R10-R13 = H, alkyl or cycloalkyl, or

NR12R13 = 3-6 membered ring containing 1 or 2 O, S or NR7 heteroatoms;

Y = OR14, SR14, C(R16)(R17)R14, C(O)R14, C(O)OR14, N(R16)C(O)R14, NC(R16)R14 or N(R16)R14;

R14 = H, alkenyl, cycloalkenyl, alkoxyalkyl, alkyl, cycloalkyl, alkylthioalkyl, alkynyl, cycloalkenylalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, hydroxyalkyl or NR18R19, and

R16-R19 = H, alkenyl, cycloalkenyl, alkoxy, alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl or heterocyclylalkyl.

INDEPENDENT CLAIMS are also included for:

(1) preparation of (I: R2 = (i); X2 = H); and

(2) regioselective preparation of a 4,5-disubstituted pyridazinone which comprises treating a compound of formula (II) with a nucleophilic agent to displace the Xa group, converting the OR98 to a leaving group and treating the compound with a second nucleophilic agent.

Xa = a leaving group, and

R98 = alkyl or aryl.

ACTIVITY - Analgesic; Antipyretic; Antiinflammatory; Antirheumatic; Antiarthritic; Osteopathic; Cytostatic; Gynecological; Antiasthmatic; Tocolytic.

MECHANISM OF ACTION - Cyclooxygenase-2 (COX-2) inhibitor; Prostaglandin endoperoxide H synthase 2 inhibitor; Prostaglandin biosynthesis inhibitor. 2-(5-Methylthien-2-ylmethyl)-4-(4-fluorophenyl)-5- (4-(methylsulfonyl)phenyl)-3(2H)-pyridazinone (Ia) was tested for inhibition of in vitro biosynthesis of prostaglandin by recombinant human COX-1 (r-hu COX-1) and recombinant human COX-2 (r-hu COX-2) enzyme assays. (Ia) Was dissolved in dimethyl sulfoxide

(3.3 volume%) and preincubated with microsomes from r-hu COX-1 and r-hu COX-2 expressed in baculovirus/Sf9 cell system, together with cofactors phenol (2 mM) and hematin (1 micro-M) for 60 minutes prior to addition of arachidonic acid (10 micro-M). The reaction was run for 2.5 minutes at room temperature, then quenched with HCl and neutralized with NaOH. Prostaglandin E2 production in the presence and absence of (Ia) was determined by enzyme immunoassay and IC50 was calculated. (Ia) Showed IC50 (in micro-M) and inhibition (in %) of r-hu COX-1/r-hu COX-2 of 100/1 and 8/100, respectively.

USE - Used for treating pain, fever, inflammation, rheumatoid arthritis, osteoarthritis and cancer (claimed), dysmenorrhea, asthma, premature labor, adhesion (e.g. pelvic adhesions), ankylosing spondylitis and other inflammatory diseases.

ADVANTAGE - (I) Are selective cyclooxygenase-2 (COX-2) inhibitors, which is an inducible isoform associated with inflammation, compared to COX-1, a constitutive isoform, required as a housekeeping enzyme in many tissues. Unwanted gastrointestinal and renal side effects, associated with the current non-steroidal antiinflammatory drugs (NSAID), are minimized.

MANUAL CODE: CPI: B05-B01D; B05-B01E; B07-D10; B14-C01; B14-C03; B14-C04; B14-C06; B14-C09; B14-D05C; B14-D10; B14-H01; B14-K01A; B14-L08; B14-N14; B14-P03; N01-A01; N07-D08A

TECH

ORGANIC CHEMISTRY - Preparation (claimed): Preparation of (I: R2 = (i); X2 = H;) comprises reacting (I: R = H) with an alkylating agent.

Preferred Compounds: The alkylating agent is of formula R99-Q.

Q = a leaving group, and

R99 = 1,1,1-trifluoroethyl, cyclopropylmethyl, 3-(2-methyl)propenyl, 4-(2-methyl)but-2-yl, 1-dichloropropen-3-yl, 2,2-dimethyl-3-oxo-4-butyl, 2,3,3,4,4,4-hexafluorobuten-1-yl, propargyl, phenylpropargyl, phenyl, phenethyl, 1-phenylpropen-3-yl, benzyl, alpha-methyl-4-fluorobenzyl, 2,3,4,5,6-pentafluorobenzyl, 4-trifluoromethoxybenacyl, 4-fluorobenzyl, 4-fluorphenyl, 2-trifluoromethylbenzyl, 2,4-difluorobenzyl, 2,4-difluorophenacyl, 4-trifluormethylphenacyl, phenacyl, 4-carboxyphenacyl, 4-chlorophenacyl, 4-cyanophenacyl, 4-diethylaminophenacyl, 3-thienylmethyl, 5-methylthien-2-ylmethyl, 5-chlorothien-2-ylmethyl, 2-benzo(b)thienylmethyl, 3-benzothienacyl, 5-chlorothiazol-2-ylmethyl, 5-methylthiazol-2-ylmethyl, 2-pyridylmethyl, 3-pyridylmethyl, 4-pyridylmethyl, quinolin-2-ylmethyl or fluoroquinolin-2-ylmethyl.

ABEX ADMINISTRATION - The dosage is 0.001-1000 (preferably 0.1-100, especially 0.01-10) mg/kg/day orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically, buccally or by inhalation (with an oral or nasal spray).

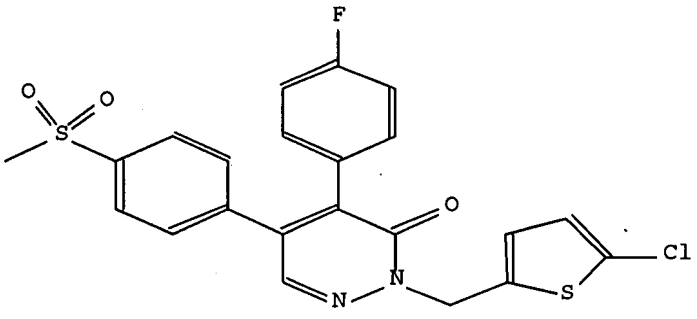
SPECIFIC COMPOUNDS - 616 Compounds (I) are specifically claimed e.g. 2-(5-methylthien-2-ylmethyl)-4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)-3(2H)-pyridazinone (Ia).

EXAMPLE - To a solution of nitrogen-unsubstituted 4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)-3(2H)-pyridazinone (0.465mmol), K2CO3 (1.4 mmol), 2-(bromomethyl)-5-methylthiophene (0.7 mmol) and NaI (catalytic) in anhydrous N,N-dimethylformamide (DMF) (10 ml) was stirred at room temperature for 18 hours. The reaction was then quenched with 2N HCl and worked up to give 2-(5-methylthien-2-ylmethyl)-4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)-3(2H)-pyridazinone (Ia).

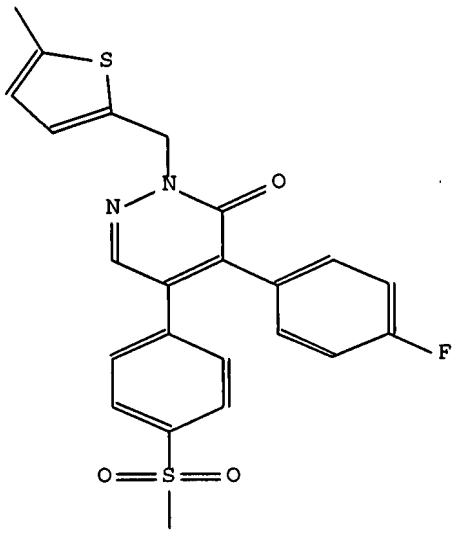
AN.S DCR-285364

CN.S 2-(5-Chloro-thiophen-2-ylmethyl)-4-(4-fluoro-phenyl)-5-(4-methanesulfonyl-phenyl)-2H-pyridazin-3-one

SDCN RA1RZ6



AN.S DCR-528585
CN.S 4-(4-Fluoro-phenyl)-5-(4-methanesulfonyl-phenyl)-2-(5-methyl-thiophen-2-ylmethyl)-2H-pyridazin-3-one
SDCN RA6SZ8



L99 ANSWER 39 OF 69 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-069781 [07] WPIX
CROSS REFERENCE: 1999-190573; 2000-350672; 2002-279861; 2002-361139; 2004-603388
DOC. NO. CPI: C2004-028957 [07]
TITLE: New pyridazinone compounds useful for treating e.g. pain, fever, inflammation, rheumatic arthritis and osteoarthritis
DERWENT CLASS: B02; B03
INVENTOR: BASHA A; BLACK L A; COGHLAN M J; KOLASA T; KORT M E; LIU H; MCCARTY C M; PATEL M; ROHDE J J; STEWART A O
PATENT ASSIGNEE: (BASH-I) BASHA A; (BLAC-I) BLACK L A; (COGH-I) COGHLAN M J; (KOLA-I) KOLASA T; (KORT-I) KORT M E; (LIUH-I) LIU H; (MCCA-I) MCCARTY C M; (PATE-I) PATEL M; (ROHD-I) ROHDE J

J; (STEW-I) STEWART A O; (ABBO-C) ABBOTT LAB

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20030225276	A1	20031204	(200407)*	EN	160[0]	C07D403-02
US 7001895	B2	20060221	(200615)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20030225276	A1 Provisional	US 1997-56733P	19970822
US 20030225276	A1 CIP of	US 1998-129570	19980805
US 20030225276	A1 CIP of	US 1998-179605	19981027
US 20030225276	A1 CIP of	US 1999-261872	19990303
US 20030225276	A1 Div Ex	US 1999-427768	19991027
US 20030225276	A1 Div Ex	US 2001-870838	20010531
US 20030225276	A1	US 2003-417959	20030417

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 20030225276	A1 Div ex	US 6307047 B

PRIORITY APPLN. INFO: US 2003-417959 20030417
US 1997-56733P 19970822
US 1998-129570 19980805
US 1998-179605 19981027
US 1999-261872 19990303
US 1999-427768 19991027
US 2001-870838 20010531

INT. PATENT CLASSIF.:
MAIN: C07D403-02
SECONDARY: C07F009-6509
IPC ORIGINAL: A61K0031-50 [I,A]; A61K0031-675 [I,A]; C07D0237-00 [I,C]; C07D0237-16 [I,A]

BASIC ABSTRACT:

US 20030225276 A1 UPAB: 20050528

NOVELTY - Pyridazinone compounds (I), their salts, esters or prodrugs are new.

DETAILED DESCRIPTION - Pyridazinone compounds of formula (I), their salts, esters or prodrugs are new.

X = O, S, NR4, NOR5a, or NNRbRc;

R4 = alkenyl, alkyl, aryl, arylalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, heterocyclic or heterocyclic alkyl;

Ra-Rc = alkyl, aryl, arylalkyl, cycloalkyl or cycloalkylalkyl;

R = alkenyl, alkoxy, alkoxyalkyl, alkoxyiminoalkoxy, alkyl, alkylcarbonylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkoxy, arylalkyl, arylhaloalkyl, arylhydroxyalkyl, aryloxy, aryloxyhaloalkyl, aryloxyhydroxyalkyl, arylcarbonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylidenealkyl, haloalkenyl, haloalkoxyhydroxyalkyl, haloalkyl, haloalkynyl, heterocyclic, heterocyclic alkoxy, heterocyclic alkyl, heterocyclic oxy, hydroxyalkyl, hydroxyiminoalkoxy, -(CH2)nC(O)R5, -(CH2)nCH(OH)R5, -(CH2)nC(NORd)R5, -(CH2)nCH(NORd)R5, -(CH2)nCH(NRdRe)R5, -

R6R7, -(CH2)nC triple bond CR7, -(CH2)n(CH(CX'3))m(CH2)pR7, -(CH2)n(CX'2)m(CH2)pR7, or (CH2)n(CHX')m(CH2)pR7;

R5 = H, (halo)alkenyl, (halo)alkyl, arylalkyl, cycloalkenyl, cycloalkyl, haloalkynyl, heterocyclic, or heterocyclic alkyl;

R6 = alkenylene or alkylene (both optionally substituted by halo);

R7, Rd, Re = H, (cyclo)alkenyl, (halo)alkyl, alkynyl, aryl, arylalkyl, cycloalkyl, heterocyclic or heterocyclic alkyl;

X' = halo;

m = 0-5;

n, p = 0-10;

R1-R3 = H, alkenyl, alkoxyalkyl, alkoxyiminoalkoxy, alkoxyiminoalkyl, alkyl, alkylcarbonylalkoxy, alkylcarbonylamino, alkylcarbonylaminoalkyl, alkynyl, aminoalkoxy, aminoalkylcarbonyloxyalkoxy aminocarbonylalkyl, aryl, arylalkenyl, arylalkyl, arylalkynyl, carboxyalkylcarbonyloxyalkoxy, cyano, cycloalkenyl, cycloalkyl, cycloalkylidenealkyl, haloalkenyloxy, haloalkoxy, haloalkyl, halo, heterocyclic, hydroxyalkoxy, hydroxyiminoalkoxy, hydroxyiminoalkyl, mercaptoalkoxy, nitro, phosphonatoalkoxy, Y or W;

W = X1-R9-benzene (substituted by X2) or thiophene (substituted by X2 and at 2-position by X1-R9);

X1 = S(O)2, S(O)(NR10), S(O), Se(O)2, P(O)(OR11), or P(O)NR12R13;

X2 = H, alkenyl, alkyl, alkynyl or halo;

R9 = (cyclo)alkenyl, alkoxy, (cyclo)alkyl, alkylamino, alkylcarbonylamino, alkynyl, amino, dialkylamino, NHNH2, or -NCHNR10R11;

R10-R13 = H, alkyl, or cycloalkyl; or

NR12R13 = 3-6 membered ring containing 1-2 O, S, or NR7;

Y = OR14, SR14, CR16R17R14, C(O)R14, C(O)OR14, NR16C(O)R14, NCR16R14, or NR16R14;

R14 = H, (cyclo)alkenyl, alkoxyalkyl, (cyclo)alkyl, alkylthioalkyl, alkynyl, cycloalkenylalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclic, heterocyclic alkyl, hydroxyalkyl, or NR18R19; and

R16-R19 = H, (cyclo)alkenyl, alkoxy, (cyclo)alkyl, aryl, arylalkyl, heterocyclic, or heterocyclic alkyl;

provided that one (and only one) of R1-R3 = W.

INDEPENDENT CLAIMS are also included for:

(1) preparation of pyridazinone derivative of formula (II) involving reacting (II; R = H) with an alkylating agent (preferably a compound of formula R'9-Q); and

(2) preparation of 4,5-disubstituted pyridazinone either involving:

(a) reacting 2H-pyridazin-3-one derivative of formula (III) with a nucleophilic agent to displace the X group;

(b) converting the -OR98 to a leaving group; and

(c) reacting (III) with a second nucleophilic agent, or reacting 4-phenyl-5H-furan-2-one derivative of formula (IV) with a hydrazine of formula RNHNH2.

R99 = alkenyl, alkoxy, alkyl, alkynyl, amino, cycloalkenyl, cycloalkyl, dialkylamino, -NHNH2 or -NCHNR10R11;

R98 = alkyl or aryl;

Q = leaving group; and

R'9 = methyl, ethyl, 1,1,1-trifluoroethyl, cyclopropylmethyl, 3-(2-methyl)propenyl, 4-(2-methyl)but-2-enyl, 1,1-dichloropropen-3-yl, 2,2-dimethyl-3-oxo-4-butyl, 2,3,3,4,4,4-hexafluorobuten-1-yl, propargyl, phenylpropargyl, phenyl, phenethyl, 1-phenylpropen-3-yl, benzyl, alpha-methyl-4-fluorobenzyl, 2,3,4,5,6-pentafluorobenzyl, 4-trifluoromethoxyphenacyl, 4-fluorobenzyl, 4-fluorophenyl, 2-trifluoromethylbenyzl, 2,4-difluorobenzyl, 2,4-difluorophenacyl, 4-trifluoromethylphenacyl, phenacyl, 4-carboxyphenacyl, 4-chlorophenacyl, 4-cyanophenacyl, 4-diethylaminophenacyl, 3-thienylmethyl, 5-methylthien-2-ylmethyl, 5-chlorothien-2-ylmethyl, 2- benzo(b)thienylmethyl, 3-benzothienacyl, 5-chlorothiazol-2-ylmethyl, 5-methylthiazol-2-ylmethyl, 2-pyridylmethyl, 3-pyridylmethyl, 4-pyridylmethyl, quinolin-2-ylmethyl, or

fluoroquinolin-2-ylmethyl (preferably 1,1,1-trifluoroethyl, benzyl, or 4-fluorophenyl).

ACTIVITY - Analgesic; Antipyretic; Antiinflammatory; Antirheumatic; Antiarthritic; Osteopathic; Cytostatic.

MECHANISM OF ACTION - Cyclooxygenase-2 (COX-2) Inhibitor; Prostaglandin Biosynthesis (preferably PGHS-1 and PGHS-2) Inhibitor.

In vitro prostaglandin biosynthesis inhibitory activity of 2-(4-fluorobenzyl)-4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)-3(2H)-pyridazinone (Ia) was evaluated using recombinant human COX-2 enzyme assay. (Ia) in dimethylsulfoxide was preincubated with microsomes from recombinant human PGHS-1 or PGHS-2 expressed in the baculovirus/Sf9 cell system as described in Gierse, J. K., Hauser, S. D., Creely, D. P., Koboldt, C., Rangwala, S., H., Isakson, P. C., and Seibert, K. Expression and selective inhibition of the constitutive and inducible forms of cyclooxygenase, Biochem J. 1995, 305: 479. (Ia) Inhibited prostaglandin biosynthesis with an IC50 of 10 nM.

USE - For treating pain, fever, inflammation, rheumatoid arthritis, osteoarthritis, adhesions and cancer (claimed).

ADVANTAGE - The compounds are potent inhibitors of cyclooxygenase-2 and PGHS-2. The selectivity of the compounds for COX-2 minimizes the unwanted gastrointestinal tract and renal side-effects as compared to non-steroidal antiinflammatory drugs. MANUAL CODE: CPI: B05-B01D; B05-B01E; B05-B01J; B05-B01M; B06-H; B07-D13; B14-C01; B14-C03; B14-C04; B14-C09; B14-D05C; B14-F04; B14-F07; B14-H01B; B14-L08

TECH

ORGANIC CHEMISTRY - Preparation: Preparation of (I; R2 = X1-R9-benzene (substituted by X2)) involves reacting (I; R = H) with an alkylating agent.

ABEX DEFINITIONS - Preferred Definitions: - R2 = W; - W = -X1-R9-benzene (substituted by X2); - X = O; - X1 = S(O)2; - R9 = NH2; - X2 = H; - R = t-butyl, 3-chlorophenyl, 3,4-difluorophenyl, 4-fluorophenyl, 4-chloro-3-fluorophenyl, 3-chloro-4-fluorophenyl, or 2,2,2-trifluoroethyl; - R1 = isobutoxy, isopentyloxy, (3-methyl-3-butenyl)oxy, 2-hydroxy-2-methyl-propoxy, 3-hydroxy-3-methylbutoxy, neopentyloxy, isopentyl, 4-fluorophenyl, 4-chlorophenyl, 4-chloro-3-fluorophenyl, 4-fluorophenyl or Y; - Y = OR14; - R14 = aryl; and - R3 = H.

ADMINISTRATION - Administration of (I) is 0.001-1000, preferably 0.1-100 mg/kg/day orally, 0.01-10 mg/kg/day parenterally, or rectally, vaginally, topically, transdermally, intraperitoneally, buccally, or nasally.

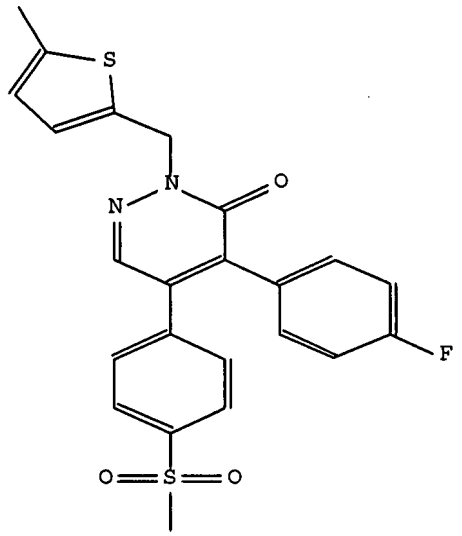
SPECIFIC COMPOUNDS - 634 Compounds (I) are specifically claimed, e.g. 2-(4-fluorobenzyl)-4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)-3(2H)-pyridazinone (Ia).

EXAMPLE - A solution of 4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)-3(2H)-pyridazinone (160 mg), potassium carbonate (193 mg), 4-fluorobenzylbromide (0.09 ml) and sodium iodide in anhydrous N,N-dimethylformamide (10 ml) were stirred at room temperature for 18 hours. The reaction mixture was quenched with 2 N HCl, extracted with ethyl acetate (2 x 20 ml), washed with brine and water, dried, filtered and concentrated to give 2-(4-fluorobenzyl)-4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)-3(2H)-pyridazinone (Ia) (110 mg).

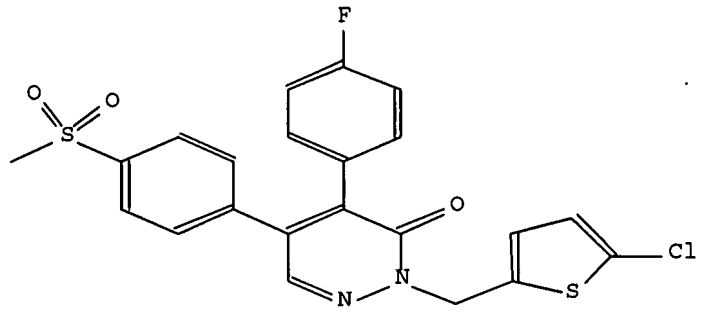
AN.S DCR-528585

CN.S 4-(4-Fluoro-phenyl)-5-(4-methanesulfonyl-phenyl)-2-(5-methyl-thiophen-2-ylmethyl)-2H-pyridazin-3-one

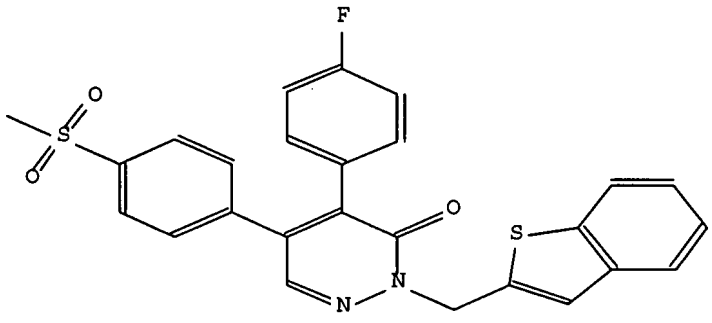
SDCN RA6SZ8



AN.S DCR-285364
CN.S 2-(5-Chloro-thiophen-2-ylmethyl)-4-(4-fluoro-phenyl)-5-(4-methanesulfonyl-phenyl)-2H-pyridazin-3-one
SDCN RA1RZ6



AN.S DCR-828750
CN.S 2-Benzo[b]thiophen-2-ylmethyl-4-(4-fluoro-phenyl)-5-(4-methanesulfonyl-phenyl)-2H-pyridazin-3-one
SDCN RACQNP



L99 ANSWER 40 OF 69 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-361139 [39] WPIX
CROSS REFERENCE: 1999-190573; 2000-350672; 2002-054478; 2002-279861; 2004-069781; 2004-603388
DOC. NO. CPI: C2002-102182 [39]
TITLE: New pyridazinone compounds, useful as selective cyclooxygenase-2 inhibitors for treating pain, fever, inflammation, rheumatoid arthritis, osteoarthritis, adhesions and cancer
DERWENT CLASS: B02; B03
INVENTOR: BASHA A; BLACK L A; COGHLAN M J; KOLASA T; KORT M E; LIU H; MCCARTY C M; PATEL M; ROHDE J J; STEWART A O
PATENT ASSIGNEE: (BASH-I) BASHA A; (BLAC-I) BLACK L A; (COGH-I) COGHLAN M J; (KOLA-I) KOLASA T; (KORT-I) KORT M E; (LIUH-I) LIU H; (MCCA-I) MCCARTY C M; (PATE-I) PATEL M; (ROHD-I) ROHDE J J; (STEW-I) STEWART A O
COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20020028938	A1	20020307	(200239)*	EN	159[0]	C07D403-02

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20020028938	A1 Provisional	US 1997-56733P	19970822
US 20020028938	A1 CIP of	US 1998-129570	19980805
US 20020028938	A1 CIP of	US 1998-179605	19981027
US 20020028938	A1 CIP of	US 1999-261872	19990303
US 20020028938	A1 Div Ex	US 1999-427768	19991027
US 20020028938	A1	US 2001-870838	20010531

PRIORITY APPLN. INFO: US 2001-870838 20010531
US 1997-56733P 19970822
US 1998-129570 19980805
US 1998-179605 19981027
US 1999-261872 19990303
US 1999-427768 19991027
INT. PATENT CLASSIF.:
MAIN: C07D403-02
SECONDARY: C07D237-14

BASIC ABSTRACT:

US 20020028938 A1 UPAB: 20050525

NOVELTY - Pyridazinone compounds (I) and their salts, esters, or prodrugs are new.

DETAILED DESCRIPTION - Pyridazinone compounds of formula (I) and their salts, esters, or prodrugs are new.

X = O, S, NR4, NORa or NNRbRc;

R4 = alkenyl, alkyl, aryl, arylalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, heterocyclic or heterocyclic alkyl;

Ra-Rc = alkyl, aryl, arylalkyl, cycloalkyl or cycloalkylalkyl;

R = alkenyl, alkoxy, alkoxyalkyl, alkoxyiminoalkoxy, alkyl, alkylcarbonylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkoxy, arylalkyl, arylalkynyl, arylhaloalkyl, arylhydroxyalkyl, aryloxy, aryloxyhaloalkyl, aryloxyhydroxyalkyl, arylcarbonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylidenealkyl, haloalkenyl, haloalkoxyhydroxyalkyl, haloalkyl, haloalkynyl, heterocyclic, heterocyclic alkoxy, heterocyclic alkyl, heterocyclic oxy, hydroxyalkyl, hydroxy-iminoalkoxy, (CH2)nC(O)R5, (CH2)nCH(OH)R5, (CH2)nC(NORd)R5, (CH2)nCH(NORd)R5, (CH2)nCH(NRdRe)R5, R6R7, (CH2)nC=CR7, (CH2)n(CH(C(X')3))(CH2)pR7, (CH2)(C(X')2)m(CH2)pR7 or (CH2)n(CHX')m(CH2)pR7;

R5 = H, alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkenyl, cycloalkyl, haloalkenyl, haloalkyl, haloalkynyl, heterocyclic or heterocyclic alkyl;

R6 = alkenylene, alkylene, halo-substituted alkenylene or halo-substituted alkylene;

R7 = H, alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkyl, cycloalkenyl, haloalkyl, heterocyclic, or heterocyclic alkyl;

Rd, Re = H, alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkenyl, cycloalkyl, haloalkyl, hetero- cyclic or heterocyclic alkyl;

X' = halo;

m = 0-5;

n = 0-10;

p = 0-10;

R1-R3 = H, alkenyl, alkoxyalkyl, alkoxyiminoalkoxy, alkoxyiminoalkyl, alkyl, alkylcarbonylalkoxy, alkylcarbonylamino, alkylcarbonylaminoalkyl, alkynyl, aminoalkoxy, aminoalkylcarbonyloxyalkoxy aminocarbonylalkyl, aryl, arylalkenyl, arylalkyl, arylalkynyl, carboxyalkylcarbonyloxyalkoxy, cyano, cycloalkenyl, cycloalkyl, cycloalkylidencalkyl, haloalkenyloxy, haloalkoxy, haloalkyl, halo, heterocyclic, hydroxyalkoxy, hydroxyiminoalkoxy, hydroxyiminoalkyl, mercaptoalkoxy, nitro, phosphonatoalkoxy, Y or W;

W = a group of formula (i) or (ii);

X1 = S(O)2 S(O)(NR10), S(O), Se(O)2, P(OXOR11) or P(O)(NR10R11);

X2 = H, alkenyl, alkyl, alkynyl or halo;

R9 = alkenyl, alkoxy, alkyl, alkylamino, alkylcarbonylamino, alkynyl, amino, cycloalkenyl, cycloalkyl, dialkylamino, NHNH2 or NCHN(R10)R11;

R10-R13 = H, alkyl or cycloalkyl; or

NR12R13 = 3-6 membered ring containing 1-2 O, S or NR7;

Y = OR14, SR14, CR16R17, C(O)R14, C(O)OR14, N(R16)C(O)R14, NC(R16)R14 or N(R16)R14;

R14 = H, alkenyl, alkoxyalkyl, alkyl, alkylthioalkyl, alkynyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclic, heterocyclic alkyl, hydroxyalkyl or NR18R19;

R16-R19 = H, alkenyl, alkoxy, alkyl, cycloalkenyl, cycloalkyl, aryl, arylalkyl, heterocyclic or heterocyclic alkyl;

provided that only one of R1-R3 is W.

INDEPENDENT CLAIMS are included for:

(1) preparation of compounds of formula (I'); and

(2) methods of regioselectively preparing 4,5-disubstituted pyridazinones.

ACTIVITY - Analgesic; Antipyretic; Antiinflammatory; Antirheumatic; Antiarthritic; Osteopathic; Cytostatic; Antiasthmatic; Tocolytic; Gynecological.

MECHANISM OF ACTION - Selective cyclooxygenase-2 (COX-2) inhibitor; Prostaglandin biosynthesis inhibitor.

In an in vitro assay to examine the inhibition of prostaglandin biosynthesis using recombinant human COX-1 (r-hu COX-1) and COX-2 (r-hu COX-2), 2-phenyl-4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)-3(2H)pyridazinone (Ia) at 10 micro M inhibited r-hu COX-2 by 97%. In comparison, (Ia) showed 0% inhibition of r-hu COX-1 at 100 micro M.

USE - For inhibiting prostaglandin biosynthesis, for treating pain, fever, inflammation, rheumatoid arthritis, osteoarthritis, adhesions, and cancer (all claimed). May also be useful for treating dysmenorrhea, asthma, premature labor, and in particular pelvic adhesions, osteoporosis, and ankylosing spondylitis.

ADVANTAGE - The selectivity of (I) avoids gastrointestinal side effects e.g. ulcers and bleeding and renal problems associated with non-steroidal antiinflammatory drugs (NSAIDs) such as ibuprofen, naproxen and fenmates which inhibit both COX-1 and COX-2. MANUAL CODE: CPI: B05-B01E; B05-B02C; B07-D10; B14-C01; B14-C03;
B14-C04; B14-C06; B14-C09; B14-D05C; B14-G02A; B14-H01; B14-K01A

TECH

ORGANIC CHEMISTRY - Preparation: In (1), preparation of (I') comprises treating a compound of formula (I'; R = H) with an alkylating agent. In (2), regioselective preparation of 4,5-disubstituted pyridazinones comprises:
(a) treating a compound of formula (IV) with a nucleophilic agent to displace the X'' group;
(b) converting the OR98 group to a leaving group; and
(c) treating the product with a second nucleophilic agent to give a 4,5-disubstituted pyridazinone.
Regioselective preparation of 4,5-disubstituted pyridazinones may also comprise treating a compound of formula (V) with a hydrazine of formula RNHNH2 to give pyridazinone compounds of formula (I'').
R98 = alkyl or aryl; and
X'' = leaving group.
Preferred Compounds: (I) are preferably of formula (I''').

ABEX ADMINISTRATION - Administration of (I) is 0.001-1000 (preferably 0.1-100) mg/kg/day orally, or 0.01-10 mg/kg parenterally, in single or divided doses. (I) May also be administered parenterally, rectally, vaginally, topically or transdermally.

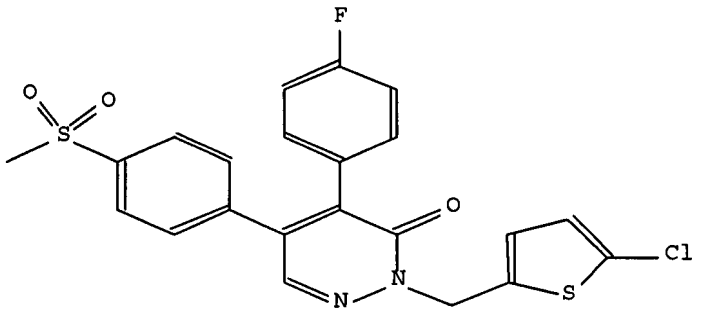
SPECIFIC COMPOUNDS - About 700 compounds (I) (including about 300 compounds (I''')) are specifically claimed, e.g. 2-phenyl-4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)-3(2H)pyridazinone (Ia).

EXAMPLE - A solution of 4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)-3(2H)-pyridazinone (160 mg), 4-fluorobenzylbromide (0.09 ml) and NaI (catalytic amount) in anhydrous dimethyl formamide (DMF; 10 ml) was stirred at room temperature for 18 hours. The reaction was quenched with 2 N HCl, extracted with ethyl acetate (2 x 20 ml) washed with brine and water, dried over MgSO4, filtered and concentrated in vacuo. The residue was purified by column chromatography (eluting with 2:2:6 ethyl acetate/dichloromethane/pentanes). Crystallization from ether/pentanes gave 2-(4-fluorophenyl)-4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)-3(2H)-pyridazinone (Ib).

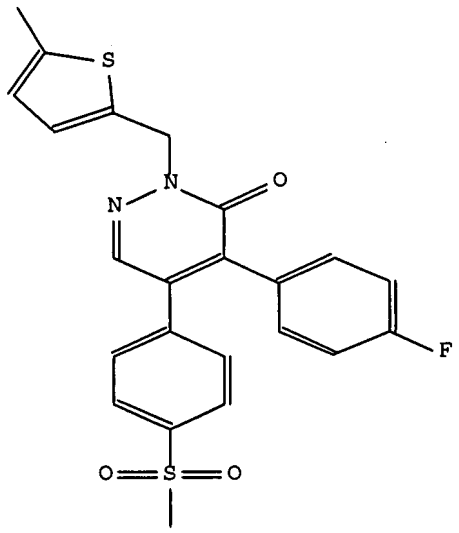
AN.S DCR-285364

CN.S 2-(5-Chloro-thiophen-2-ylmethyl)-4-(4-fluoro-phenyl)-5-(4-methanesulfonyl-phenyl)-2H-pyridazin-3-one

SDCN RA1RZ6



AN.S DCR-528585
CN.S 4-(4-Fluoro-phenyl)-5-(4-methanesulfonyl-phenyl)-2-(5-methyl-thiophen-2-ylmethyl)-2H-pyridazin-3-one
SDCN RA6SZ8



L99 ANSWER 41 OF 69 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-279861 [32] WPIX
CROSS REFERENCE: 1999-190573; 2000-350672; 2002-054478; 2002-361139; 2004-069781; 2004-603388
DOC. NO. CPI: C2002-082271 [32]
TITLE: New pyridazinones useful in the treatment of cyclooxygenase mediated diseases e.g. pain
DERWENT CLASS: B03
INVENTOR: BASHA A; BLACK L A; COGHLAN M J; KOLASA T; KORT M E; LIU H; MCCARTY C M; PATEL M; ROHDE J J; STEWART A O
PATENT ASSIGNEE: (BASH-I) BASHA A; (BLAC-I) BLACK L A; (COGH-I) COGHLAN M J; (KOLA-I) KOLASA T; (KORT-I) KORT M E; (LIUH-I) LIU H;

(MCCA-I) MCCARTY C M; (PATE-I) PATEL M; (ROHD-I) ROHDE J J; (STEW-I) STEWART A O

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20020013318	A1	20020131	(200232)*	EN	159[0]	A61K031-50

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20020013318	A1 Provisional	US 1997-56733P	19970822
US 20020013318	A1 CIP of	US 1998-129570	19980805
US 20020013318	A1 CIP of	US 1998-179605	19981027
US 20020013318	A1 CIP of	US 1999-261872	19990303
US 20020013318	A1 Div Ex	US 1999-427768	19991027
US 20020013318	A1	US 2001-871195	20010531

PRIORITY APPLN. INFO: US 2001-871195 20010531
US 1997-56733P 19970822
US 1998-129570 19980805
US 1998-179605 19981027
US 1999-261872 19990303
US 1999-427768 19991027

INT. PATENT CLASSIF.:
MAIN: A61K031-50
SECONDARY: C07D237-14

BASIC ABSTRACT:

US 20020013318 A1 UPAB: 20050525

NOVELTY - Pyridazinone derivatives (I) are new.

DETAILED DESCRIPTION - Pyridazinones of formula (I), their salts, ester or prodrugs are new.

X = O, S, -NR4, -NORa or -NNRbRc;

R4 = alkenyl, alkyl, aryl, arylalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl or heterocyclic(alkyl);

Ra, Rb and Rc = alkyl, aryl, arylalkyl, cycloalkyl or cycloalkylalkyl;

R = alkenyl, alkoxy, alkoxyalkyl, alkoxyiminoalkoxy, alkyl, arylalkenyl, arylalkoxy, arylalkyl, arylalkynyl, arylhaloalkyl, aryloxyhydroxyalkyl, arylcarbonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylidenealkyl, haloalkenyl, haloalkoxyhydroxyalkyl, haloalkyl, haloalkynyl, heterocyclic, heterocyclic alkoxy, heterocyclic alkyl, heterocyclic oxy, hydroxyalkyl, hydroxyiminoalkoxy, -(CH2)nC(O)R5, -(CH2)nCH(OH)R5, -(CH2)nC(NORd)R5, -(CH2)nCH(NORd)R5, -(CH2)nCH(NRdRe)R5, -R6R7, -(CH2)nCCR7, -(CH2)n(CH(CX'3))m(CH2)pR7, -(CH2)n(CX'2)-m(CH2)pR7 or -(CH2)n(CHX')m(CH2)pR7;

R5 = R7, haloalkenyl or haloalkynyl;

R6 = alkenylene or alkylene (both optionally substituted by halogen);

R7, Rd and Re = H, (cyclo)alkenyl, (cyclo)alkyl, alkynyl, aryl, arylalkyl, haloalkyl or heterocyclic(alkyl);

X' = halogen;

m = 0 - 5;

n = 0 - 10;

p = 0 - 10;

R1 - R3 = H, alkenyl, alkoxyalkyl, alkoxyiminoalkoxy, alkoxyiminoalkyl, alkyl, alkylcarbonylalkoxy, alkylcarbonylamino, alkylcarbonylaminoalkyl, alkynyl, aminoalkoxy, aminoalkylcarbonyloxyalkoxy, aminocarbonylalkyl, aryl,

arylalkenyl, arylalkyl, arylalkynyl, carboxyalkylcarbonyloxyalkoxy, cyano, cycloalkenyl, cycloalkyl, cycloalkylidenealkyl, haloalkenyloxy, haloalkoxy, haloalkyl, halogen, heterocyclic, hydroxyalkoxy, hydroxyiminoalkoxy, hydroxyiminoalkyl, mercaptoalkoxy, nitro, phosphonatoalkoxy, Y or W;

W = T'-X1-R9;

T' = 1,4-phenylene or 2,5-thiophenylene (both substituted by X2);

X1 = S(O)2, S(O)(NR10), S(O), Se(O)2, P(O)(OR11) or P(O)(NR12R13);

X2 = H, alkenyl, alkyl, alkynyl, halogen;

R9 = alkenyl, alkoxy, alkyl, alkylamino, alkylcarbonylamino, alkynyl, amino, cycloalkenyl, cycloalkyl, dialkylamino, -NHNH2 or -NCHN(R10)R11;

R10 - R13 = H or (cyclo)alkyl;

NR12R13 = 3 - 6 membered ring containing 1 or 2 heteroatoms selected from O, S or NR7;

Y = -OR14, -SR14, -C(R16)(R17)R14, -C(O)R14, -C(O)OR14, -N(R16)C(O)R14, -NC(R16)R14 or -N(R16)R14;

R14 = H, (cyclo)alkenyl, alkoxyalkyl, (cyclo)alkyl, alkylthioalkyl, alkynyl, cycloalkenylalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclic(alkyl), hydroxyalkyl or NR18R19;

R16 - R19 = H, (cyclo)alkenyl, alkoxy, (cyclo)alkyl, aryl, arylalkyl or heterocyclic(alkyl).

provided that at least one (preferably only one) of R1 - R3 must be W.

INDEPENDENT CLAIMS are also included for

(1) preparation of a compound of formula (III) by treating a compound of formula (III) (where R = H) with an alkylating agent;

(2) regioselective preparation of a 4,5-disubstituted pyridazinone involving either

(i) treating a compound of formula (IV) with a nucleophilic agent to displace the X' group;

(ii) converting the -OR98 to a leaving group; and

(iii) treating the compound with a second nucleophilic agent to form the 4,5-disubstituted pyridazinone, or treating a compound of formula (V) with a hydrazine of formula R'NHNH2; and

(3) a compound of formula (VI), its salt, ester or prodrug.

R'9 = (cyclo)alkenyl, alkoxy, (cyclo)alkyl, alkynyl, amino, dialkylamino, -NHNH2 or -NCHN(R10)R11;

R' = alkenyl, alkoxy, alkoxyalkyl, alkyl, alkylcarbonylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkoxy, arylalkyl, arylalkynyl, arylhaloalkyl, aryloxyhydroxyalkyl, aryloxy, aryloxyhaloalkyl, aryloxyhydroxyalkyl, arylcarbonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, haloalkenyl, haloalkoxyhydroxyalkyl, haloalkyl, haloalkynyl, heterocyclic, heterocyclic alkoxy, heterocyclic alkyl, heterocyclic oxy, hydroxyalkyl, -(CH2)nC(O)R'5, -(CH2)nCH(OH)R'5, -(CH2)nC(NORd)R'5, -(CH2)nCH(NORd)R'5, -(CH2)nCH(NRdRe)R'5, -R6R7, -(CH2)nCCR7, -(CH2)n(CH(CX'3))m(CH2)pR7, -(CH2)n(CX'2)m(CH2)pR7 or -(CH2)n(CHX')m(CH2)pR7;

R'5 = R5 (except H);

R'1 and R'3 = H, alkenyl, alkoxyalkyl, alkyl, alkynyl, alkylcarbonylalkoxy, alkylcarbonylamino, alkylcarbonylaminoalkyl, aminoalkoxy, aminocarbonylalkyl, aryl, arylalkenyl, arylalkyl, arylalkynyl, cyano, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylidenealkyl, haloalkenyloxy, haloalkoxy, haloalkyl, halogen, heterocyclic (alkyl), hydroxyalkoxy, hydroxyalkylamino, hydroxyalkylthio, mercaptoalkoxy, nitro or Y';

Y' = -OR'14, -SR'14, -C(R16)(R17)R'14, -C(O)R'14, -C(O)OR'14, -N(R16)C(O)R'14, -NC(R16)R'14 or -N(R16)R'14;

R'14 = R14 (except hydroxyalkyl).

R98 = alkyl or aryl;

X' = leaving group.

R = alkyl, aryl, arylalkyl, haloalkyl or haloalkenyl;

R1 = alkoxy, aminoalkylcarbonyloxyalkoxy, carboxyalkylcarbonyloxyalkoxy, hydroxyalkoxy, hydroxyalkyl or phosphonatoalkoxy;

R9 = alkyl, alkylcarbonylamino or amino.

ACTIVITY - Analgesic; antipyretic; antiinflammatory; antirheumatic; antiarthritic; osteopathic; cytostatic.

MECHANISM OF ACTION - Prostaglandin biosynthesis (particularly prostaglandin endoperoxide H synthase (PGHS-2, cyclooxygenase-2, COX-2) protein) inhibitor.

Carrageenan induced air pouch prostaglandin biosynthesis model (CAP) study was carried out on male sprague dawley rats by injecting 20 ml of sterile air on day 0. Three days later the pouch was reinflated with an additional 10 ml of sterile air. On day 7, 1 nanoliter of saline containing 0.2% lambda carrageenan was injected into the pouch to induce inflammatory reaction by the release of prostaglandins. 2-(3,4-difluorophenyl)-4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)- 3(2H)-pyridazinone was dosed at 3 mg/kg body weight, 30 minutes prior to carrageenan. 4 hours after the carrageenan injection the pouch was lavaged and levels of prostaglandins determined. The result indicated 98% inhibition of prostaglandin biosynthesis by the test compound.

USE - For the treatment of pain, fever, inflammation, rheumatoid arthritis, osteoarthritis, adhesions and cancer (claimed). The compounds are also useful in the treatment of cyclooxygenase mediated diseases, premature labor, osteoporosis and ankylosing spondolitis.

ADVANTAGE - The compounds are selective inhibitors of PGHS-2, have no side-effects and minimize stomach toxicity. MANUAL CODE: CPI: B07-D13; B14-C01; B14-C03; B14-C04; B14-C09A; B14-C09B; B14-D08; B14-H01; B14-N01; B14-N14

TECH

ORGANIC CHEMISTRY - Preferred Compounds: The alkylating agent is of formula R99-Q.

R99 = methyl, ethyl, 1,1,1-trifluoroethyl, cyclopropylmethyl, 3-(2-methyl)propenyl, 4-(2-methyl)but-2-enyl, 1,1-dichloropropen-3-yl, 2,2-dimethyl-3-oxo-4-butyl, 2,3,3,4,4,4-hexafluorobuten-1-yl, propargyl, phenylpropargyl, phenyl, phenethyl, 1-phenylpropen-3-yl, benzyl, ortho-methyl-4-fluorobenzyl, 2,3,4,5,6-pentafluorobenzyl, 4-trifluoromethoxyphenacyl, 4-fluorobenzyl, 4-fluorophenyl, 2-trifluoromethylbenzyl, 2,4-difluorobenzyl, 2,4-difluorophenacyl, 4-trifluoromethylphenacyl, phenacyl, 4-carboxyphenacyl, 4-chlorophenacyl, 4-cyanophenacyl, 4-diethylaminophenacyl, 3-thienylmethyl, 5-methylthien-2-ylmethyl, 5-chlorothien-2-ylethyl, 2-benzo(b)thienylmethyl, 3-benzothienacyl, 5-chlorothiazol-2-ylmethyl, 5-methylthiazol-2-ylethyl, 2-pyridylmethyl, 3-pyridylmethyl, 4-pyridylethyl, quinolin-2-ylmethyl or fluoroquinolin-2-ylmethyl (preferably 1,1,1-trifluoroethyl, phenyl, benzyl, alpha-methyl-4-fluorobenzyl, 4-fluorobenzyl, 4-fluorophenyl or 2,4-difluorobenzyl, especially 1,1,1-trifluoroethyl, benzyl or 4-fluorophenyl);

Q = leaving group.

ABEX DEFINITIONS - Preferred Definitions - R2 = W; - T' = 1,4-phenylene; - X1 = SO2; - R9 = methyl or amino; - X2 = H or fluorine (preferably H); - R = tert-butyl, 3-chlorophenyl, 3,4-difluorophenyl, 4-fluorophenyl, 4-chloro-3-fluorophenyl, 3-chloro-4-fluorophenyl or 2,2,2-trifluoroethyl; - R1 = isobutoxy, isopentyloxy, (3-methyl-3-butenyl)oxy, 2-hydroxy-2-methyl-propoxy, 3-hydroxy-3-methylbutoxy, neopentyloxy, isopentyl, 4-fluorophenyl, 4-chlorophenyl, 4-chloro-3-fluorophenyl, 4-fluorophenoxy or Y; - Y = -OR14; - R14 = aryl; - R3 = H; - R = tert-butyl, haloalkyl, phenyl (optionally mono- or di-substituted by chlorine or fluorine); - R1 = (hydroxy)alkoxy or phosphonatoalkoxy; - R'9 = methyl or amino.

ADMINISTRATION - The compounds are administered orally, subcutaneously,

intramuscularly, rectally, vaginally or transdermally. Dosage is 0.001 - 1000 (preferably 0.1 - 100) mg/kg body weight/day for oral administration.

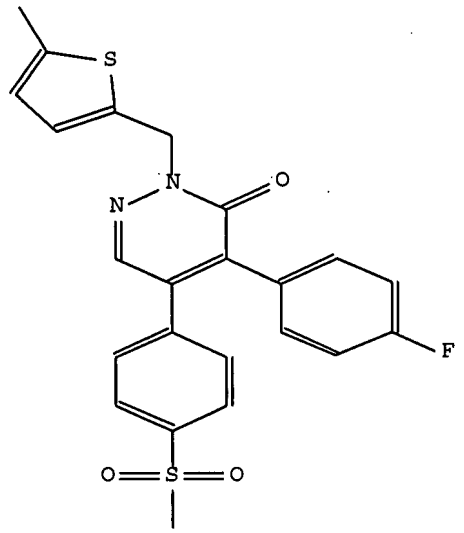
SPECIFIC COMPOUNDS - 621 compounds are specifically claimed as (I). e.g. 2-(3,4-difluorophenyl)-4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)-3(2H)-pyridazinone.

EXAMPLE - A mixture of 4-(4-fluorophenyl)-5-(4-(methylsulfonyl)-3(2H)-pyridazinone (172 mg), Cu powder (32 mg), anhydrous K2CO3 (207 mg) and 3,4-difluorobromobenzene (0.12 ml) was prepared in pyridine (20 ml). The solution was stirred at reflux for 14 hours. The mixture was then cooled and partitioned between water and ethyl acetate. The acetate layer was washed with 10% citric acid, water, brine and concentrated in vacuum to obtain 2-(3,4-difluorophenyl)-4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl-3(2H)-pyridazinone (yield 70%).

AN.S DCR-528585

CN.S 4-(4-Fluoro-phenyl)-5-(4-methanesulfonyl-phenyl)-2-(5-methyl-thiophen-2-ylmethyl)-2H-pyridazin-3-one

SDCN RA6SZ8



L99 ANSWER 42 OF 69 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2001-488639 [53] WPIX

CROSS REFERENCE: 2001-465209; 2001-475871; 2001-514302; 2001-514303; 2001-514320; 2001-522009; 2002-352118

DOC. NO. CPI: C2001-146647 [53]

TITLE: Use of pyridazino quinolinedione compounds for treating a subject e.g. human suffering from pain, especially neuropathic pain

DERWENT CLASS: B02

INVENTOR: BARE T; BARE T M; BROWN D G; BROWN D G A; HORCHLER C L; HORCHLER C L A; MURPHY M; MURPHY M A; STEELMAN G B; STEELMAN G B A; URBANEK R A; URBANEK R A A; XIAO W; XIAO W A; BARE M

PATENT ASSIGNEE: (ASTR-C) ASTRAZENECA AB; (BARE-I) BARE T M; (BROW-I) BROWN D G; (HORC-I) HORCHLER C L; (MURP-I) MURPHY M;

(STEE-I) STEELMAN G B; (URBA-I) URBANEK R A; (XIAO-I) XIAO W

COUNTRY COUNT: 93

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2001047924	A1	20010705	(200153)*	EN	57[0]	
AU 2001024200	A	20010709	(200164)	EN		
EP 1244660	A1	20021002	(200265)	EN		
JP 2003519146	W	20030617	(200349)	JA	77	C07D471-04
US 20030181449	A1	20030925	(200364)	EN		
EP 1244660	B1	20060322	(200622)	EN		
DE 60026883	E	20060511	(200634)	DE		
DE 60026883	T2	20061123	(200678)	DE		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001047924	A1	WO 2000-SE2607	20001219
DE 60026883	E	DE 2000-626883	20001219
EP 1244660	A1	EP 2000-987932	20001219
EP 1244660	B1	EP 2000-987932	20001219
DE 60026883	E	EP 2000-987932	20001219
EP 1244660	A1	WO 2000-SE2607	20001219
JP 2003519146	W	WO 2000-SE2607	20001219
US 20030181449	A1	WO 2000-SE2607	20001219
EP 1244660	B1	WO 2000-SE2607	20001219
DE 60026883	E	WO 2000-SE2607	20001219
AU 2001024200	A	AU 2001-24200	20001219
JP 2003519146	W	JP 2001-549394	20001219
US 20030181449	A1	US 2003-168761	20030224
DE 60026883	T2	DE 2000-626883	20001219
DE 60026883	T2	EP 2000-987932	20001219
DE 60026883	T2	WO 2000-SE2607	20001219

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
DE 60026883	E	Based on	EP 1244660	A
AU 2001024200	A	Based on	WO 2001047924	A
EP 1244660	A1	Based on	WO 2001047924	A
JP 2003519146	W	Based on	WO 2001047924	A
EP 1244660	B1	Based on	WO 2001047924	A
DE 60026883	E	Based on	WO 2001047924	A
DE 60026883	T2	Based on	EP 1244660	A
DE 60026883	T2	Based on	WO 2001047924	A

PRIORITY APPLN. INFO: US 2000-236881P 20000929
US 1999-171906P 19991223
US 2003-168761 20030224

INT. PATENT CLASSIF.:

MAIN: C07D471-04

SECONDARY: A61K031-5025; A61K031-5377; A61P025-04

IPC ORIGINAL: A61K0031-5025 [I,A]; A61K0031-5025 [I,A]; A61K0031-5025 [I,C]; C07D0471-00 [I,C]; C07D0471-00 [I,C]; C07D0471-04 [I,A]; C07D0471-04 [I,A]

IPC RECLASSIF.: A61K0031-502 [I,A]; A61K0031-502 [I,C]; A61K0031-5025 [I,A]; A61K0031-5025 [I,C]; A61K0031-503 [I,A]; A61K0031-503 [I,C]; A61K0031-5375 [I,C]; A61K0031-5377 [I,A]; A61K0031-541 [I,A]; A61K0031-541 [I,C]; A61P0025-00 [I,C]; A61P0025-04 [I,A]; C07D0471-00 [I,C]; C07D0471-04 [I,A]; C07D0487-00 [I,C]; C07D0487-04 [I,A]

BASIC ABSTRACT:

WO 2001047924 A1 UPAB: 20060117

NOVELTY - Treating a subject suffering from pain involves administering pyridazino quinoline dione compounds (I).

DETAILED DESCRIPTION - Treating a subject suffering from pain involves administering pyridazino quinoline dione compounds of formula (I).

A = (CH2)n;

n = 0-4;

R1 = halo;

D-E = group of formula (i);

R2 = H, OH, halo, 1-4C alkyl, 1-4C alkoxy, hydroxy 2-6C alkynyl, 1-3C alkyl OC(O)O, 1-3C alkyl S(O)m, benzimidazolyl, C(O)NR3R4, NR3R4 or NHC(O)NR3R4;

m = 0-2;

R3, R4 = H, 1-4C alkyl, 1-4C alkoxy, (CH2)n'O1-4C alkyl, 1-3C alkylfuranyl, cyclohexyl or phenyl; or

NR3R4 = morpholinyl, piperazinyl or pyrrolidinyl; and

n' = 1-4;

provided that at least one of R2 is not H.

An INDEPENDENT CLAIM is also included for the preparation of (I) involving: (i) reacting ketone/aldehyde ED-C(O)-R with BocNHNH2 in the presence of tetrahydrofuran or MeOH to give ED-C(NNHBoc)-R (II), where (II) is either hydrogenated using 10%Pd/C at 40 psi for 2-18 hours or reduced to give Boc-protected hydrazine (Boc)N(H)N(H)ADE (III), or EDAX is reacted to give the Boc-protected hydrazine. Alternatively an alternative hydrazine is prepared by reacting an aromatic aldehyde H-C(O)DCO2H with NH2NHBoc to give HC(=NNHBoc)DCO2H which is further reacted with DPPA, PhMe and R3R4NH and heated to give HC(=NNHBoc)DNC(O)-NR3R4 (IV). (IV) is reacted with ammonium formate in the presence of 10% Pd/C catalyst to give NNHBoc-C-D-N-C(O)NR3R4; or ii) coupling (III) with 1-cyclohexyl-3-(2-morpholinoethyl)carbodiimide or other coupling reagent and cyclizing the product.

ACTIVITY - Analgesic.

MECHANISM OF ACTION - N-methyl-D-aspartate (NMDA) receptor activity inhibitor.

Binding of 7-chloro-4-hydroxy-2-(4-(3-proparginol)phenyl)-1,2,5,10-tetrahydropyridazino(4,5-b)quinoline-1,10-dione (Ib) to the N-methyl-D-aspartate (NMDA) receptor glycine site is assessed by measuring the ability of (Ib) to inhibit the binding of tritiated MDL105, 519 to brain membranes bearing the receptor. The potency (Ki) of (A) is found to be 1.0 nM.

USE - In prophylactic treatment of pain (claimed) or nociception particularly for the amelioration of neuropathic pain in mammals e.g. humans.

MANUAL CODE: CPI: B06-D17; B14-C01; B14-L06; N02-F01

TECH

ORGANIC CHEMISTRY - Preparation: (Boc)N(H)N(H)AD is obtained by the hydrogenation of the corresponding imine at 40 psi for 2-18 hours or by hydride mediated reduction. The hydrazine is coupled with 4-hydroxy-2-pyrrolidine carbonyl-quinoline-3-carboxylic acid using 1-cyclohexyl-3-(2-morpholinoethyl)carbodiimide metho-para-toluenesulfonate or other coupling agent to form a bis amide which was cyclized intermolecularly with methanesulfonic acid as room-temperature in tetrahydrofuran to form (I).

ABEX DEFINITIONS - Preferred Definitions: - n = 1; - R1 = Cl; - R2 = H, OH, bromo, iodo, methyl, ethyl, methoxy, ethoxy, hydroxyproparginyl, methylcarboxylate, methylthio, benzimidazole-5-yl, dimethylamino,

NHC(O)NR3R4 or OC(O)NR3R4; - R3, R4 = H, methyl, ethyl, methoxy, (CH2)2O-1-2C alkyl, methylfuran-2-yl, cyclohexyl or phenyl.

ADMINISTRATION - The compound can be administered orally, topically, parenterally, buccally, nasally, vaginally or rectally or by inhalation. No dosage given.

SPECIFIC COMPOUNDS - 28 Compounds (I) are specifically claimed e.g. 7-chloro-4-hydroxy-2-((3-(piperazinylcabonyl)phenyl)methyl)-1,2,5,10-tetrahydropyridazino(4,5-b)quinoline-1,10-dione methanesulfonate (Ia).

EXAMPLE - To a slurry of 7-chloro-4-oxo-2-(pyrrolidinylcarbonyl)hydroquinoline-3-carboxylic acid (0.65 g) in dichloromethane (DCM) (40 ml) was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.44 g) and stirred for 5 minutes. To the mixture was added a solution of (tert-butoxy)-N-(3-(1-piperazinylcarbonyl)phenyl)methyl)amino)carboxamide (0.93 g) and 4-(dimethylamino)pyridine (DMAP) (0.02 g) in DCM (10 ml), refluxed for 4 hours, cooled and diluted with DCM (50 ml). The DCM was extracted, dried over MgSO4 and the solvent was removed to give N-((tert-butoxy)carbonylamino)(7-chloro-4-oxo-2-(pyrrolidinylcarbonyl)(3-hydroquinolyl)-N-((3-(1-piperazinylcarbonyl)phenyl)methylcarboxamide (86%). To a solution of this compound (1.3 g) in tetrahydrofuran (THF) (30 ml) was added methanesulfonic acid (4 ml) and stirred overnight. The volatiles were removed and to the residual oil was added diethyl ether (200 ml). The mixture was stirred and then allowed to settle into two layers. To the oil was added water (5 ml), followed by sodium chloride. The precipitate formed was filtered, washed and sonicated in 20 ml of 5/1 diethyl ether/methyl alcohol for 15 minutes. The material was filtered, washed and dried to give 7-chloro-4-hydroxy-2-((3-(piperazinylcarbonyl)phenyl)methyl)-1,2,5,10-tetrahydropyridazino(4,5-b)quinoline-1,10-dione methanesulfonate (44%).

=> d ibib ab fhit 43
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX, WPIX, MEDLINE, EMBASE, DRUGU, MARPAT' - CONTINUE? (Y)/N:y

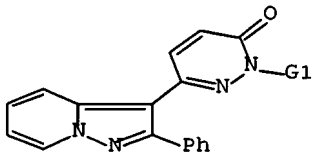
L99 ANSWER 43 OF 69 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 135:107325 MARPAT Full-text
TITLE: Preparation of pyrazolopyridines as adenosine antagonists and their use for treatment of various diseases
INVENTOR(S): Akabane, Atsushi; Kuroda, Satoshi; Itani, Hiromichi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 22 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001192384	A	20010717	JP 2000-378350	20001213
PRIORITY APPLN. INFO.:			AU 1999-4622	19991213

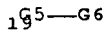
AB Pyrazolopyridines I [R = lower alkenyl- or aryl-substituted lower alkyl (linked by O), AR1; R1 = substituted oxadiazolyl, thiazolyl, oxazolyl, imidazolyl; A = lower alkylene] or their salts are prepared by N-substitution of I (R = H), cyclocondensation of I [R = AC(NH2):NOH; A = same as above] with R2COX2 (R2 = lower alkyl; X2 = leaving group), etc. Thus, 2.88 g I (R = H) was treated with NaH and allyl bromide at room temperature for 2 h in DMF to give

2.04 g I (R = allyl), which inhibited binding of [3H]DPCPX to A1 receptor, and [3H]CGS21680 to A2a receptor with Ki values of 0.04 and 2.69 nM, resp.

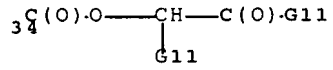
MSTR 1

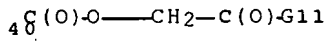


G1 = alkenyl <containing 2-6 C> /
alkyl <containing 1-6 C> (substd. by 1 or more G2) / **19** /
(Specifically claimed: CH2CH=CH2)

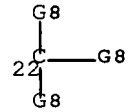


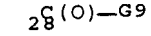
G2 = aryl (opt. substd. by 1 or more G3) /
alkoxy <containing 1-6 C> (opt. substd. by G4) /
(Specifically claimed: Ph)
G3 = R / (Examples: Cl / Br / F / I /
alkyl <containing 1-6 C> / alkoxy <containing 1-6 C> / OH /
NO2)
G4 = aryl (opt. substd. by 1 or more G3)
G5 = alkylene <containing 1-6 C> /
(Specifically claimed: CH2)
G6 = oxadiazolyl (opt. substd. by 1 or more G7) /
thiazolyl (opt. substd. by 1 or more G7) /
oxazolyl (opt. substd. by 1 or more G7) /
imidazolyl (opt. substd. by 1 or more G7) / 34 / 40 /
(Specifically claimed: CO2H)





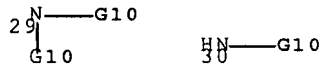
G7 = alkyl <containing 1-6 C> (opt. substd. by CO2H) /
acyl / **aryl** / pyridyl / 22 / CO2H /
(Specifically claimed: Ph / pyridyl / 28 / CH2OH)





G8 = Cl / Br / F / I

G9 = NH2 / 29 / 30 / heterocycle <attached through 1 or more N>



G10 = alkyl <containing 1-6 C> (opt. substd. by dialkylamino <each alkyl containing 1-6 C>) / aryl (opt. substd. by 1 or more G3)
G11 = alkyl <containing 1-6 C> / Ph
Derivative: or salts
Patent location: claim 1

=> d ibib ed ab ind 44-69
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX, WPIX, MEDLINE, EMBASE, DRUGU, MARPAT' - CONTINUE? (Y)/N:y

L99 ANSWER 44 OF 69 MEDLINE on STN
ACCESSION NUMBER: 1998358188 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9691090
TITLE: **Phosphodiesterase** 3 inhibitors suppress oocyte maturation and consequent pregnancy without affecting ovulation and cyclicity in rodents.
AUTHOR: Wiersma A; Hirsch B; Tsafriri A; Hanssen R G; Van de Kant M; Kloosterboer H J; Conti M; Hsueh A J
CORPORATE SOURCE: Department of Pharmacology, N.V. Organon, P.O. Box 20, 5340 BH Oss, The Netherlands.. a.wiersma@organon.oss.akzonobel.nl
CONTRACT NUMBER: P50 HD31398 (NICHD)
SOURCE: The Journal of clinical investigation, (1998 Aug 1) Vol. 102, No. 3, pp. 532-7.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 3 Sep 1998
Last Updated on STN: 3 Mar 2000
Entered Medline: 26 Aug 1998
ED Entered STN: 3 Sep 1998
Last Updated on STN: 3 Mar 2000
Entered Medline: 26 Aug 1998
AB During each reproductive cycle, a preovulatory surge of gonadotropins induces meiotic maturation of the oocyte in the preovulatory follicle followed by ovulation. Although gonadotropins stimulate cAMP production in somatic cells of the follicle, a decrease in intra-oocyte cAMP levels is required for resumption of meiosis in oocytes. Based on the observed compartmentalization of the cAMP-degrading enzyme, **phosphodiesterase**, in follicular somatic and germ cells, inhibitors of **phosphodiesterase** 3 were used to block meiosis in ovulating oocytes in rodents. By this strategy, we demonstrated that fertilization and pregnancy could be prevented without disturbing follicle rupture and normal estrous cyclicity. In contrast to conventional

contraceptive pills that disrupt ovarian steroidogenesis and reproductive cycles, the present strategy achieves effective contraception by selective blockage of oocyte maturation and development without alterations in ovulation and reproductive cyclicity.

CT Check Tags: Female
1-Methyl-3-isobutylxanthine: PD, pharmacology
***3',5'-Cyclic-Nucleotide Phosphodiesterase: AI, antagonists & inhibitors**
Animals
Comparative Study
*Contraceptive Agents, Female: PD, pharmacology
*Cyclic AMP: PH, physiology
*Estrus: DE, drug effects
Fertilization: DE, drug effects
Heart Rate: DE, drug effects
Hypoxanthine: PD, pharmacology
Isoenzymes: AI, antagonists & inhibitors
*Meiosis: DE, drug effects
Menotropins: PD, pharmacology
Mice
Mice, Inbred C57BL
Milrinone
*Oogenesis: DE, drug effects
Ovarian Follicle: DE, drug effects
Ovarian Follicle: PH, physiology
*Ovulation: DE, drug effects
Ovulation Induction
***Phosphodiesterase Inhibitors: PD, pharmacology**
Pregnancy
Purinones: PD, pharmacology
Pyridazines: PD, pharmacology
Pyridones: PD, pharmacology
Pyrrolidinones: PD, pharmacology
Quinolones: PD, pharmacology
Rats
Rats, Sprague-Dawley
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Rolipram
*Second Messenger Systems: PH, physiology
Substrate Specificity
Thiophenes: PD, pharmacology

RN 129425-83-8 (Org 9935); 28822-58-4 (1-Methyl-3-isobutylxanthine); 37762-06-4 (zaprinast); 60-92-4 (Cyclic AMP); 61413-54-5 (Rolipram); 61489-71-2 (Menotropins); 68-94-0 (Hypoxanthine); 68550-75-4 (cilostamide); 74150-27-9 (pimobendan); 78415-72-2 (Milrinone)

CN 0 (Contraceptive Agents, Female); 0 (Isoenzymes); 0 (**Phosphodiesterase** Inhibitors); 0 (Purinones); 0 (Pyridazines); 0 (Pyridones); 0 (Pyrrolidinones); 0 (Quinolones); 0 (**Thiophenes**); EC 3.1.4.- (**phosphodiesterase** III); EC 3.1.4.17 (3',5'-Cyclic-Nucleotide **Phosphodiesterase**)

L99 ANSWER 45 OF 69 MEDLINE on STN
ACCESSION NUMBER: 1998365599 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9700242
TITLE: Pharmacologic agents inhibit rat mesangial cell proliferation and collagen synthesis.
AUTHOR: Fang C C; Yen C J; Shyu R S; Wu M S; Tsai T J; Hsieh B S
CORPORATE SOURCE: Department of Emergency Medicine, College of Medicine, National Taiwan University, Taipei, Taiwan.

SOURCE: Journal of the Formosan Medical Association = Taiwan yi zhi, (1998 Jul) Vol. 97, No. 7, pp. 458-64.
Journal code: 9214933. ISSN: 0929-6646.
PUB. COUNTRY: TAIWAN: Taiwan, Province of China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 3 Sep 1998
Last Updated on STN: 3 Sep 1998
Entered Medline: 27 Aug 1998
ED Entered STN: 3 Sep 1998
Last Updated on STN: 3 Sep 1998
Entered Medline: 27 Aug 1998

AB Prevention of the development of end-stage renal disease is one of the most promising areas of research in nephrology. Because mesangial cell proliferation and extracellular matrix accumulation have been regarded as antecedents of glomerulosclerosis, agents that can inhibit mesangial cell proliferation may have a potential to retard the progression of renal diseases. Therefore, we investigated several clinically available agents that might affect mesangial cell proliferation and collagen synthesis in male Sprague-Dawley rats. Cell proliferation was measured by the tetrazolium dye uptake method. Collagen synthesis was measured by 3H-proline incorporation into pepsin-resistant, salt-precipitated collagen. Intracellular cAMP levels were measured by enzyme immunoassay. Our results showed that hydralazine (82% inhibition at 10 micrograms/mL), ticlopidine (61% inhibition at 30 micrograms/mL), aminophylline (66% inhibition at 200 micrograms/mL), and nicametate (91% inhibition at 1 mg/mL) inhibited serum-stimulated rat mesangial cell (RMC) growth in a dose-dependent manner. Ticlopidine (43% inhibition at 30 mg/mL), aminophylline (52% inhibition at 200 mg/mL), and nicametate (35% inhibition at 1 mg/mL) inhibited collagen synthesis in confluent RMCs. Aminophylline may act through increasing intracellular cAMP levels (9.7 +/- 0.7 pmol/mg protein at 200 micrograms/mL of aminophylline vs 4.2 +/- 0.6 pmol/mg protein at control). These data suggest that aminophylline, ticlopidine, hydralazine, and nicametate can inhibit RMC proliferation and collagen synthesis.

CT Check Tags: Male
Aminophylline: PD, pharmacology
Analysis of Variance
Animals
*Cardiovascular Agents: PD, pharmacology
*Collagen: BI, biosynthesis
*Collagen: DE, drug effects
*Glomerular Mesangium: CY, cytology
*Glomerular Mesangium: DE, drug effects
Hydralazine: PD, pharmacology
Nicotinic Acids: PD, pharmacology
Rats
Rats, Sprague-Dawley
Research Support, Non-U.S. Gov't
Ticlopidine: PD, pharmacology
RN 1641-74-3 (nicametate); 317-34-0 (Aminophylline); 55142-85-3 (Ticlopidine); 86-54-4 (Hydralazine); 9007-34-5 (Collagen)
CN 0 (Cardiovascular Agents); 0 (Nicotinic Acids)

L99 ANSWER 46 OF 69 MEDLINE on STN
ACCESSION NUMBER: 96031070 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8564209
TITLE: Effects of type-selective **phosphodiesterase** inhibitors on glucose-induced insulin secretion and islet

phosphodiesterase activity.

AUTHOR: Shafiee-Nick R; Pyne N J; Furman B L
CORPORATE SOURCE: Department of Physiology and Pharmacology, University of Strathclyde, Glasgow.
SOURCE: British journal of pharmacology, (1995 Aug) Vol. 115, No. 8, pp. 1486-92.
Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 15 Mar 1996
Last Updated on STN: 3 Mar 2000
Entered Medline: 4 Mar 1996
ED Entered STN: 15 Mar 1996
Last Updated on STN: 3 Mar 2000
Entered Medline: 4 Mar 1996

AB 1. We examined various type-selective **phosphodiesterase** (PDE) inhibitors on glucose-induced insulin secretion from rat isolated islets, on islet PDE activity and on islet cyclic AMP accumulation in order to assess the relationship between type-selective PDE inhibition and modification of insulin release. 2. The non-selective PDE inhibitor, 3-isobutyl-1-methylxanthine (IBMX, 10(-5)-10(-3) M), as well as the type III selective PDE inhibitors SK&F 94836 (10(-5)-10(-3) M), Org 9935 (10(-7)-10(-4) M), SK&F 94120 (10(-5)-10(-4) M) and ICI 118233 (10(-6)-10(-4) M) each caused concentration-dependent augmentation (up to 40% increase) of insulin release in the presence of a stimulatory glucose concentration (10 mM), but not in the presence of 3 mM glucose. 3. Neither the type IV PDE inhibitor rolipram (10(-4) M) nor the type I and type V PDE inhibitor, zaprinast (10(-4)-10(-3) M) modified glucose-induced insulin release when incubated with islets, although a higher concentration of rolipram (10(-3) M) inhibited secretion by 55%. However, when islets were preincubated with these drugs followed by incubation in their continued presence, zaprinast (10(-6)-10(-4) M) produced a concentration-dependent inhibition (up to 45% at 10(-4) M). Under these conditions, rolipram inhibited insulin secretion at a lower concentration (10(-4) M) than when simply incubated with islets. 4. A combination of SK&F 94836 (10(-5) M) and forskolin (5 x 10(-8) M) significantly augmented glucose-induced insulin secretion (30% increase), although neither drug alone, in these concentrations, produced any significant effect.(ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Male
1-Methyl-3-isobutylxanthine: PD, pharmacology
3',5'-Cyclic-Nucleotide Phosphodiesterase: AI, antagonists & inhibitors
Analysis of Variance
Animals
Cyclic AMP: ME, metabolism
Dose-Response Relationship, Drug
Drug Interactions
Forskolin: PD, pharmacology
*Glucose: PD, pharmacology
Guanidines: PD, pharmacology
*Insulin: SE, secretion
*Islets of Langerhans: DE, drug effects
Islets of Langerhans: ME, metabolism
*Isoenzymes: ME, metabolism
***Phosphodiesterase Inhibitors: PD, pharmacology**
*Phosphoric Diester Hydrolases: ME, metabolism
Purinones: PD, pharmacology

Pyrazines: PD, pharmacology
Pyridazines: PD, pharmacology
Pyrrolidinones: PD, pharmacology
Rats
Rats, Sprague-Dawley
Rolipram
Thiophenes: PD, pharmacology

RN 11061-68-0 (Insulin); 115344-47-3 (siguazodan); 129425-83-8 (Org 9935); 28822-58-4 (1-Methyl-3-isobutylxanthine); 37762-06-4 (zaprinast); 50-99-7 (Glucose); 60-92-4 (Cyclic AMP); 61413-54-5 (Rolipram); 66428-89-5 (Forskolin); 89541-55-9 (5-(4-acetamidophenyl)pyrazin-2(1H)-one); 93851-00-4 (ICI 118233)

CN 0 (Guanidines); 0 (Isoenzymes); 0 (**Phosphodiesterase** Inhibitors); 0 (Purinones); 0 (Pyrazines); 0 (Pyridazines); 0 (Pyrrolidinones); 0 (**Thiophenes**); EC 3.1.4 (Phosphoric Diester Hydrolases); EC 3.1.4.17 (3',5'-Cyclic-Nucleotide **Phosphodiesterase**)

L99 ANSWER 47 OF 69 MEDLINE on STN
ACCESSION NUMBER: 94361704 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7521642
TITLE: Synergistic interactions between selective pharmacological inhibitors of **phosphodiesterase** isozyme families PDE III and PDE IV to attenuate proliferation of rat vascular smooth muscle cells.
AUTHOR: Pan X; Arauz E; Krzanowski J J; Fitzpatrick D F; Polson J B
CORPORATE SOURCE: Department of Pharmacology and Therapeutics, College of Medicine, University of South Florida, Tampa 33612-4799.
SOURCE: Biochemical pharmacology, (1994 Aug 17) Vol. 48, No. 4, pp. 827-35.
Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 13 Oct 1994
Last Updated on STN: 3 Mar 2000
Entered Medline: 30 Sep 1994

ED Entered STN: 13 Oct 1994
Last Updated on STN: 3 Mar 2000
Entered Medline: 30 Sep 1994

AB The interaction between selective inhibitors of 3',5'-cyclic-nucleotide **phosphodiesterase** (PDE) III (cyclic GMP inhibited **phosphodiesterase**) and selective inhibitors of PDE IV (Ro 20-1724 inhibited **phosphodiesterase**) to attenuate fetal bovine serum-stimulated incorporation of [3H]thymidine into DNA and cell proliferation was studied in a line (A10) of vascular smooth muscle cells (VSMC). The nonselective PDE inhibitors 3-isobutyl-1-methylxanthine (IBMX) and papaverine attenuated DNA synthesis with EC50 values (16 and 18 microM, respectively) in the same range as their published IC50 values (2-50 and 2-25 microM, respectively) as PDE inhibitors. The selective PDE III inhibitors CI-930 and cilostamide used alone attenuated DNA synthesis with EC50 values (> 300 and 5.3 microM, respectively) that were much higher than published IC50 values (0.15-0.46 and 0.005-0.064 microM, respectively) for inhibition of PDE III. In the presence of the PDE IV inhibitor rolipram (10 microM), their EC50 values were shifted (0.66 and 0.16 microM, respectively) much closer to their respective IC50 values. When the selective PDE IV inhibitors rolipram and Ro 20-1724 were used alone, they attenuated DNA synthesis with EC50 values (111 and > 100 microM, respectively) much higher than their IC50 values (0.6-2.6 and 2-13 microM, respectively) as inhibitors

of PDE IV, but 10 microM CI-930 (PDE III inhibitor) shifted their EC50 values (0.56 and 1.5 microM, respectively) much closer to their IC50 values. In experiments that assessed VSMC proliferation using the MTT [3-(4,5-**dimethylthiazol** -2-yl)-2, 5-diphenyltetrazolium bromide] method, IBMX and papaverine attenuated proliferation with EC50 values (27 and 58 microM, respectively) close to their IC50 values. CI-930 and cilostamide used alone did not cause 50% attenuation of proliferation at the highest concentrations tested (100 and 10 microM, respectively). In the presence of 5 microM rolipram, however, their effects were enhanced greatly with EC50 values (0.86 and 0.23 microM, respectively) that were close to their IC50 values as PDE III inhibitors. Similarly, rolipram and Ro 20-1724 attenuated VSMC proliferation with EC50 values close to their IC50 values in the presence (2.1 and 4.6 microM, respectively) but not in the absence (> 100 and > 10 microM, respectively) of 2 microM CI-930. The interactions between PDE III inhibitors and PDE IV inhibitors to attenuate DNA synthesis and VSMC proliferation were synergistic as determined by the combination index. The data demonstrate that the synergistic interactions that attenuate incorporation of [3H]thymidine into DNA are accompanied by synergistic attenuations of VSMC division.(ABSTRACT TRUNCATED AT 400 WORDS)

CT **1-Methyl-3-isobutylxanthine: PD, pharmacology**
Animals
Cell Division: DE, drug effects
Cell Line
Comparative Study
Drug Synergism
Isoenzymes: AI, antagonists & inhibitors
Models, Chemical
*Muscle, Smooth, Vascular: EN, enzymology
***Phosphodiesterase Inhibitors: PD, pharmacology**
*Phosphoric Diester Hydrolases: ME, metabolism
Pyridazines: PD, pharmacology
Pyrrolidinones: PD, pharmacology
Quinolones: PD, pharmacology
Rats
Research Support, Non-U.S. Gov't
Rolipram
Thymidine: ME, metabolism

RN 28822-58-4 (1-Methyl-3-isobutylxanthine); 50-89-5 (Thymidine); 61413-54-5 (Rolipram); 68550-75-4 (cilostamide); 86798-59-6 (4,5-dihydro-6-(4-(imidazol-1-yl)phenyl)-5-methyl-3(2H)-pyridazinone)

CN 0 (Isoenzymes); 0 (**Phosphodiesterase** Inhibitors); 0 (Pyridazines); 0 (Pyrrolidinones); 0 (Quinolones); EC 3.1.4 (Phosphoric Diester Hydrolases)

L99 ANSWER 48 OF 69 MEDLINE on STN
ACCESSION NUMBER: 91115456 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1703513
TITLE: A method for evaluating anti-allergic drugs by simultaneously induced passive cutaneous anaphylaxis and mediator cutaneous reactions.
AUTHOR: Koda A; Miura T; Inagaki N; Sakamoto O; Arimura A; Nagai H; Mori H
CORPORATE SOURCE: Department of Pharmacology, Gifu Pharmaceutical University, Japan.
SOURCE: International archives of allergy and applied immunology, (1990) Vol. 92, No. 3, pp. 209-16.
Journal code: 0404561. ISSN: 0020-5915.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199103
ENTRY DATE: Entered STN: 29 Mar 1991
Last Updated on STN: 29 Jan 1996
Entered Medline: 6 Mar 1991
ED Entered STN: 29 Mar 1991
Last Updated on STN: 29 Jan 1996
Entered Medline: 6 Mar 1991
AB Homologous passive cutaneous anaphylaxis (PCA) was induced by IgE antibody and, simultaneously, cutaneous reactions were induced by some allergic mediators such as histamine, serotonin and leukotriene (LT) C4 on rat back skin. Disodium cromoglycate and tranilast with inhibitory actions on mediator release inhibited PCA specifically, whereas antihistaminics, including ketotifen, azelastine, mequitazine and diphenhydramine, inhibited histamine- and serotonin-induced cutaneous reactions as well as PCA. Anti-slow-reacting substance of anaphylaxis drugs, KC-404 and FPL-55712, significantly inhibited PCA and histamine- and serotonin-induced reactions, but at the same doses they did not produce significant inhibition of the LTC4-induced reaction. All reactions tested were strongly inhibited dose dependently with the beta stimulants, salbutamol and isoproterenol, and a xanthine derivative, theophylline, which are known to increase the intracellular cyclic AMP level. We think that this method enables the determination of the properties of anti-allergic drugs.
CT Check Tags: Female; Male
Albuterol: PD, pharmacology
Animals
Anthranilic Acids: PD, pharmacology
Diphenhydramine: PD, pharmacology
Dose-Response Relationship, Drug
*Histamine H1 Antagonists: PD, pharmacology
Isoproterenol: PD, pharmacology
Ketotifen: PD, pharmacology
*Passive Cutaneous Anaphylaxis: DE, drug effects
Phenothiazines: PD, pharmacology
Phthalazines: PD, pharmacology
Rats
Rats, Inbred Strains
Skin Tests
Theophylline: PD, pharmacology
RN 18559-94-9 (Albuterol); 29216-28-2 (mequitazine); 34580-13-7 (Ketotifen); 53902-12-8 (tranilast); 58-55-9 (Theophylline); 58-73-1 (Diphenhydramine); 58581-89-8 (azelastine); 7683-59-2 (Isoproterenol)
CN 0 (Anthranilic Acids); 0 (Histamine H1 Antagonists); 0 (Phenothiazines); 0 (Phthalazines)

L99 ANSWER 49 OF 69 MEDLINE on STN
ACCESSION NUMBER: 90119968 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2575358
TITLE: Inhibitory effect of adenine nucleotides and anti-allergic drugs on phosphorylation of phosphatidylinositol in rat mast cell granules.
AUTHOR: Kurosawa M; Okayama Y; Kobayashi S
CORPORATE SOURCE: First Department of Internal Medicine, Gunma University School of Medicine, Japan.
SOURCE: Allergy, (1989 Nov) Vol. 44, No. 8, pp. 576-81.
Journal code: 7804028. ISSN: 0105-4538.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199002
ENTRY DATE: Entered STN: 28 Mar 1990
Last Updated on STN: 6 Feb 1998
Entered Medline: 12 Feb 1990
ED Entered STN: 28 Mar 1990
Last Updated on STN: 6 Feb 1998
Entered Medline: 12 Feb 1990
AB Rat mast cell granules were obtained by sonication of highly purified rat mast cells and isolated in a Percoll gradient. Phosphorylation of endogenous phosphatidylinositol in rat mast cell granules, which is catalyzed by phosphatidylinositol kinase in the granules, was assayed by measuring the incorporation of 32P from [gamma 32P]ATP into phosphatidylinositol 4-phosphate. Lipids were isolated with methanol/chloroform/HCl and were separated by thin-layer chromatography on oxalic acid impregnated silica gel plates. Phosphatidylinositol 4-phosphate areas were identified by staining with iodine, scraped and measured for 32P radioactivity. The phosphorylation reaction was inhibited by 50-500 microM adenosine, ADP and 500 microM AMP in a concentration-dependent manner. Among several anti-allergic drugs investigated. 100-1000 microM theophylline and 10-100 microM azelastine inhibited the phosphorylation reaction, but disodium cromoglycate and ketotifen had little effect.
CT 1-Phosphatidylinositol 4-Kinase
*Adenine Nucleotides: PD, pharmacology
Adenosine: PD, pharmacology
Adenosine Diphosphate: PD, pharmacology
Adenosine Monophosphate: PD, pharmacology
Animals
Cromolyn Sodium: PD, pharmacology
*Cytoplasmic Granules: ME, metabolism
Histamine H1 Antagonists: PD, pharmacology
Ketotifen: PD, pharmacology
*Mast Cells: ME, metabolism
Mast Cells: UL, ultrastructure
*Phosphatidylinositols: ME, metabolism
Phosphorylation
Phosphotransferases: AI, antagonists & inhibitors
Phthalazines: PD, pharmacology
Rats
Theophylline: PD, pharmacology
RN 15826-37-6 (Cromolyn Sodium); 34580-13-7 (Ketotifen); 58-55-9 (Theophylline); 58-61-7 (Adenosine); 58-64-0 (Adenosine Diphosphate); 58581-89-8 (azelastine); 61-19-8 (Adenosine Monophosphate)
CN 0 (Adenine Nucleotides); 0 (Histamine H1 Antagonists); 0 (Phosphatidylinositols); 0 (Phthalazines); EC 2.7 (Phosphotransferases); EC 2.7.1.67 (1-Phosphatidylinositol 4-Kinase)

L99 ANSWER 50 OF 69 MEDLINE on STN
ACCESSION NUMBER: 89390254 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2571246
TITLE: The effect of azelastine and some other antiasthmatic and antiallergic drugs on calmodulin and protein kinase C.
AUTHOR: Middleton E Jr; Ferriola P; Drzewiecki G; Sofia R D
CORPORATE SOURCE: Department of Medicine State University of New York, Buffalo 14214.
SOURCE: Agents and actions, (1989 Aug) Vol. 28, No. 1-2, pp. 9-15. Journal code: 0213341. ISSN: 0065-4299.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 9 Mar 1990
Last Updated on STN: 6 Feb 1995
Entered Medline: 26 Oct 1989
ED Entered STN: 9 Mar 1990
Last Updated on STN: 6 Feb 1995
Entered Medline: 26 Oct 1989
AB The antiallergic and antiasthmatic drug, azelastine, interacts strongly with calmodulin (but not bovine serum albumin) as determined by an indirect assay; it also moderately inhibited the Ca2+-calmodulin-dependent enzyme bovine brain **phosphodiesterase.** Ketotifen was less active than azelastine in both assays of calmodulin reactivity and both drugs were less active than the recognized calmodulin inhibitor, W-7. Neither azelastine nor ketotifen had any inhibitory effect on the Ca2+- and phospholipid-dependent protein kinase C. A number of other commonly employed antiallergic and antiasthmatic drugs were essentially inactive in the calmodulin assays and had no or marginal inhibitory effect on protein kinase C.
CT **3',5'-Cyclic-Nucleotide Phosphodiesterase: AI, antagonists & inhibitors**
Animals
Brain: EN, enzymology
Calcium: PD, pharmacology
*Calmodulin: AI, antagonists & inhibitors
Calmodulin: PD, pharmacology
Comparative Study
Fluorescent Dyes
*Histamine H1 Antagonists: PD, pharmacology
Ketotifen: PD, pharmacology
Phosphodiesterase Inhibitors
***Phthalazines: PD, pharmacology**
*Protein Kinase C: AI, antagonists & inhibitors
***Pyridazines: PD, pharmacology**
Rats
Serum Albumin, Bovine: ME, metabolism
Spectrometry, Fluorescence
Sulfonamides: PD, pharmacology
RN 34580-13-7 (Ketotifen); 58581-89-8 (azelastine); 65595-90-6 (W 7); 7440-70-2 (Calcium)
CN 0 (Calmodulin); 0 (Fluorescent Dyes); 0 (Histamine H1 Antagonists); 0 (**Phosphodiesterase** Inhibitors); 0 (Phthalazines); 0 (Pyridazines); 0 (Serum Albumin, Bovine); 0 (Sulfonamides); EC 2.7.1.37 (Protein Kinase C); EC 3.1.4.17 (3',5'-Cyclic-Nucleotide **Phosphodiesterase**)

L99 ANSWER 51 OF 69 MEDLINE on STN
ACCESSION NUMBER: 89157873 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2466139
TITLE: Therapeutic aspects of intractable asthma.
AUTHOR: Tomioka S; Kuroiwa H
SOURCE: Nihon Ky bu Shikkan Gakkai zasshi, (1988 Mar) Vol. 26, No. 3, pp. 242-7.
Journal code: 7505737. ISSN: 0301-1542.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198904
ENTRY DATE: Entered STN: 6 Mar 1990
Last Updated on STN: 29 Jan 1999
Entered Medline: 13 Apr 1989
ED Entered STN: 6 Mar 1990

Last Updated on STN: 29 Jan 1999
Entered Medline: 13 Apr 1989
CT Check Tags: Female; Male
Adult
Aged
Anthranilic Acids: PK, pharmacokinetics
Anthranilic Acids: TU, therapeutic use
*Asthma: DT, drug therapy
Cromolyn Sodium: PK, pharmacokinetics
Cromolyn Sodium: TU, therapeutic use
English Abstract
Humans
Ketotifen: TU, therapeutic use
Middle Aged
Phthalazines: TU, therapeutic use
Terbutaline: AA, analogs & derivatives
Terbutaline: PK, pharmacokinetics
Theophylline: PK, pharmacokinetics
RN 15826-37-6 (Cromolyn Sodium); 23031-25-6 (Terbutaline); 34580-13-7 (Ketotifen); 41570-61-0 (tulobuterol); 53902-12-8 (tranilast); 58-55-9 (Theophylline); 58581-89-8 (azelastine)
CN 0 (Anthranilic Acids); 0 (Phthalazines)

L99 ANSWER 52 OF 69 MEDLINE on STN
ACCESSION NUMBER: 85260072 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2410374
TITLE: Inhibition of allergic histamine release by azelastine and selected antiallergic drugs from rabbit leukocytes.
AUTHOR: Chand N; Pillar J; Diamantis W; Sofia R D
SOURCE: International archives of allergy and applied immunology, (1985) Vol. 77, No. 4, pp. 451-5.
Journal code: 0404561. ISSN: 0020-5915.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198509
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 6 Feb 1995
Entered Medline: 16 Sep 1985
ED Entered STN: 20 Mar 1990
Last Updated on STN: 6 Feb 1995
Entered Medline: 16 Sep 1985
AB The ability of azelastine to inhibit allergic histamine release from rabbit mixed leukocytes was studied and compared with selected antiallergic drugs. Azelastine, ketotifen, diphenhydramine, theophylline and disodium cromoglycate (DSCG) produced concentration-dependent inhibition of allergic histamine release from rabbit basophils. The concentrations inhibiting histamine release by 50% (IC50; microM) were as follows: azelastine = 4.5; ketotifen = 9.5; diphenhydramine = 18.9; theophylline = 56.9; DSCG = greater than 1,000. DSCG was added to the cells immediately prior to antigen challenge. All other drugs were preincubated for a period of 10 min prior to antigen challenge. At the IC50 level, azelastine is about 2, 4, 13 and greater than 200 times as effective as ketotifen, diphenhydramine, theophylline and DSCG, respectively. The IC50 of azelastine following 0, 10 and 30 min preincubation were 2.4, 1.9 and 3.5 microM, respectively. These observations showed: (1) azelastine is capable of acting rapidly on basophils and of inhibiting allergic histamine secretion, and (2) the prolongation of the preincubation time of azelastine up to 30 min with rabbit leukocytes did not exhibit any sign of tachyphylaxis (loss of activity). In conclusion, azelastine is a potent inhibitor of

allergic histamine secretion from the leukocytes of ragweed-sensitized rabbits.

CT Check Tags: Male
Animals
Comparative Study
Cromolyn Sodium: PD, pharmacology
Diphenhydramine: PD, pharmacology
*Histamine H1 Antagonists: PD, pharmacology
*Histamine Release: DE, drug effects
In Vitro
Ketotifen: PD, pharmacology
*Leukocytes: DE, drug effects
Leukocytes: IM, immunology
***Phthalazines: PD, pharmacology**
***Pyridazines: PD, pharmacology**
Rabbits
Theophylline: PD, pharmacology
Time Factors

RN 15826-37-6 (Cromolyn Sodium); 34580-13-7 (Ketotifen); 58-55-9 (Theophylline); 58-73-1 (Diphenhydramine); 58581-89-8 (azelastine)

CN 0 (Histamine H1 Antagonists); 0 (Phthalazines); 0 (Pyridazines)

L99 ANSWER 53 OF 69 MEDLINE on STN
ACCESSION NUMBER: 86022470 . MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2413739
TITLE: Inhibition of IgE-mediated allergic histamine release from rat peritoneal mast cells by azelastine and selected antiallergic drugs.
AUTHOR: Chand N; Pillar J; Diamantis W; Sofia R D
SOURCE: Agents and actions, (1985 Jul) Vol. 16, No. 5, pp. 318-22. Journal code: 0213341. ISSN: 0065-4299.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198511
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 21 Mar 1990
Entered Medline: 18 Nov 1985

ED Entered STN: 21 Mar 1990
Last Updated on STN: 21 Mar 1990
Entered Medline: 18 Nov 1985

AB The ability of azelastine to inhibit IgE-mediated allergic histamine release from the peritoneal mast cells of actively sensitized rats was investigated and compared with selected antiallergic agents. Azelastine added simultaneously with the allergic stimuli (ovalbumin, OA, 10 micrograms/ml + phosphatidylserine, PS, 10 micrograms/ml) or preincubated with cells for 10 min prior to antigen challenge produced similar concentration-dependent inhibition of allergic histamine release. The IC50s (microM) following 10-min preincubation were as follows: azelastine = 4.8; astemizole = 86.3; ketotifen = 112.2; diphenhydramine = 133 and theophylline = 2040.3. At IC50 level azelastine was about 18, 23, 28 and 425 times as effective as astemizole, ketotifen (newer histamine H1-receptor antagonists), diphenhydramine (a traditional H1-receptor antagonist), and theophylline (a **phosphodiesterase** inhibitor), respectively. Sodium cromoglycate in a concentration range or 1-1000 microM (0 or 10-min preincubation) failed to exert any inhibitory effect. These data showed that among six drugs tested azelastine is the most potent inhibitor of allergic histamine release from rat peritoneal mast cells.

CT Check Tags: Male
Animals

Astemizole
Benzimidazoles: PD, pharmacology
Comparative Study
Diphenhydramine: PD, pharmacology
*Histamine Release: DE, drug effects
Hypersensitivity: IM, immunology
*Hypersensitivity: PP, physiopathology
*Immunoglobulin E: PH, physiology
Ketotifen: PD, pharmacology
*Mast Cells: SE, secretion
Ovalbumin: IM, immunology
Phosphatidylserines: IM, immunology
***Phthalazines: PD, pharmacology**
***Pyridazines: PD, pharmacology**
Rats
Rats, Inbred Strains
Theophylline: PD, pharmacology
RN 34580-13-7 (Ketotifen); 37341-29-0 (Immunoglobulin E); 58-55-9 (Theophylline); 58-73-1 (Diphenhydramine); 58581-89-8 (azelastine); 68844-77-9 (Astemizole); 9006-59-1 (Ovalbumin)
CN 0 (Benzimidazoles); 0 (Phosphatidylserines); 0 (Phthalazines); 0 (Pyridazines)

L99 ANSWER 54 OF 69 MEDLINE on STN
ACCESSION NUMBER: 85052505 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6094309
TITLE: Adverse drug reactions in the elderly: case studies.
AUTHOR: Clark B G; Vestal R E
SOURCE: Geriatrics, (1984 Dec) Vol. 39, No. 12, pp. 53-4, 60-3, 66.
Journal code: 2985102R. ISSN: 0016-867X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198501
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 20 Mar 1990
Entered Medline: 14 Jan 1985
ED Entered STN: 20 Mar 1990
Last Updated on STN: 20 Mar 1990
Entered Medline: 14 Jan 1985
AB ADRs in the elderly may present in an atypical manner. Atypical reactions are uncommon and usually cannot be anticipated from the chemical or pharmacologic properties of the drug. In many cases, you may find a careful and thorough drug history and knowledge of drug-related reactions more helpful than an array of laboratory data.
CT Check Tags: Female; Male
Acetazolamide: AE, adverse effects
*Aged
Anemia, Hemolytic: CI, chemically induced
Bromocriptine: AE, adverse effects
Captopril: AE, adverse effects
Chlorpropamide: AE, adverse effects
Cimetidine: AE, adverse effects
Clonidine: AE, adverse effects
Dienestrol: AE, adverse effects
*Drug Therapy: AE, adverse effects
Humans
Hydralazine: AE, adverse effects

Lung Diseases: CI, chemically induced
Middle Aged
Nitrofurantoin: AE, adverse effects
Pancreatitis: CI, chemically induced
Papaverine: AE, adverse effects
Peripheral Nervous System Diseases: CI, chemically induced
Procainamide: AE, adverse effects
Propranolol: AE, adverse effects
Sulindac: AE, adverse effects
Theophylline: AE, adverse effects
Timolol: AE, adverse effects

RN 25614-03-3 (Bromocriptine); 26839-75-8 (Timolol); 38194-50-2 (Sulindac); 4205-90-7 (Clonidine); 51-06-9 (Procainamide); 51481-61-9 (Cimetidine); 525-66-6 (Propranolol); 58-55-9 (Theophylline); 58-74-2 (Papaverine); 59-66-5 (Acetazolamide); 62571-86-2 (Captopril); 67-20-9 (Nitrofurantoin); 84-17-3 (Dienestrol); 86-54-4 (Hydralazine); 94-20-2 (Chlorpropamide)

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ACCESSION NUMBER: 2006040376 EMBASE Full-text
TITLE: Synthesis of original trifluoromethylated 6-aryl-**pyridazines** fused with **thiazolidine** or 1,2,4-triazole.
AUTHOR: Brule C.; Bouillon J.-P.; Nicolai E.; Portella C.
CORPORATE SOURCE: C. Portella, Laboratoire Reactions Selectives et Applications' Associe au CNRS (UMR 6519), Universite de Reims Champagne-Ardenne, Faculte des Sciences, B.P. 1039, 51687 Reims Cedex 2, France. charles.portella@univ-reims.fr
SOURCE: Synthesis, (5 Jan 2006) No. 1, pp. 103-106. .
Refs: 14
ISSN: 0039-7881 CODEN: SYNTBF
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 Feb 2006
Last Updated on STN: 9 Feb 2006

ED Entered STN: 9 Feb 2006
Last Updated on STN: 9 Feb 2006

AB An efficient synthesis of original 8-trifluoromethyl-7H-**thiazolo** [3,2-b]-and 1,2,4-triazolo[4,3-b]pyridazines is described. Starting from the 4-trifluoromethyl-4,5-dihydropyridazin-3-one, the methodology involves a five-membered ring closure, based on the reaction of a bis(electrophilic) reagent with an exocyclic heteroatom linked to position 3 and the endocyclic nitrogen at position 2 of the pyridazine nucleus. .COPYRGT. Georg Thieme Verlag Stuttgart.

CT Medical Descriptors:
*drug synthesis
*pharmacophore
substitution reaction
reduction
stereochemistry
amidation
ring closing metathesis
oxidation
infrared spectroscopy
proton nuclear magnetic resonance
carbon nuclear magnetic resonance

mass spectrometry
article
Drug Descriptors:
***pyridazine derivative: AN, drug analysis**
***pyridazine derivative: DV, drug development**
***thiazolidine derivative: AN, drug analysis**
***thiazolidine derivative: DV, drug development**
*1,2,4 triazole derivative: AN, drug analysis
*1,2,4 triazole derivative: DV, drug development
***8 trifluoromethyl 7h thiazolo[3,2 b]pyridazine: AN, drug analysis**
***8 trifluoromethyl 7h thiazolo[3,2 b]pyridazine: DV, drug development**
*8 trifluoromethyl 1,2,4 triazolo[4,3 b]pyridazine: AN, drug analysis
*8 trifluoromethyl 1,2,4 triazolo[4,3 b]pyridazine: DV, drug development
*fluorinated hydrocarbon: AN, drug analysis
*fluorinated hydrocarbon: DV, drug development
4 trifluoromethyl 4,5 dihydropyridazin 3 one
pyridazinone derivative
heterocyclic nitro compound
6 (4' bromophenyl) 8 trifluoromethyl 7h thiazolo[3,2 d]pyridazin 3 one: AN, drug analysis
6 (4' bromophenyl) 8 trifluoromethyl 7h thiazolo[3,2 d]pyridazin 3 one: DV, drug development
6 (4' bromophenyl) 3 methyl 8 trifluoromethyl 1,2,4 triazolo[4,3 b]pyridazine : AN, drug analysis
6 (4' bromophenyl) 3 methyl 8 trifluoromethyl 1,2,4 triazolo[4,3 b]pyridazine : DV, drug development
6 (4' bromophenyl) 8 trifluoromethyl 1,2,4 triazolo[4,3 b]pyridazin 3 one: AN, drug analysis
6 (4' bromophenyl) 8 trifluoromethyl 1,2,4 triazolo[4,3 b]pyridazin 3 one: DV, drug development
3 amino 6 (4' bromophenyl) 8 trifluoromethyl 1,2,4 triazolo[4,3 b]pyridazine : AN, drug analysis
3 amino 6 (4' bromophenyl) 8 trifluoromethyl 1,2,4 triazolo[4,3 b]pyridazine : DV, drug development
unclassified drug

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ACCESSION NUMBER: 2006038115 EMBASE Full-text
TITLE: Facile route for the synthesis of **pyridazine** derivatives: Unexpected pathway to **benzothiazole**, benzimidazole, and triazole derivatives.
AUTHOR: El Rady E.A.
CORPORATE SOURCE: E.A. El Rady, Chemistry Department, Faculty of Science, South Valley University, Aswan, Egypt. emanelradi@hotmail.com
SOURCE: Synthetic Communications, (1 Feb 2006) Vol. 36, No. 1, pp. 37-49. .
Refs: 11
ISSN: 0039-7911 CODEN: SYNCAV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 Feb 2006
Last Updated on STN: 9 Feb 2006
ED Entered STN: 9 Feb 2006
Last Updated on STN: 9 Feb 2006

AB 4-Amino-5-arylmethylidene-3-phenyl-pyridazin-6-ones 7 have been synthesized and reacted with selected nucleophile reagents such as phenyl hydrazine, semicarbazide, semithiocarbazide, cyanoacetohydrazide, 2- **aminothiophenol**, and 2-phenylenediamine in ethanol triethyl-amine solution. An unexpected 1-phenyl-3-arylaziridene 10, 3-aryl-5-oxo(thio)- 1,2,4-triazole 21, 4-amino-3-aryl-6-hydroxy-pridazine 27, 2- **arylbenzothiazole** 30a-c, and 2-arylbenzimidazole 30d-f have been obtained, respectively. Also, 2-**aminothiophenol** and 2-phenylenediamine were reacted with N-phenylmethylidene-2-cyanoacetohydrazide 2, affording the new 1,4-benzodiazepine derivatives 35. Copyright .COPYRGT. Taylor & Francis LLC.

CT Medical Descriptors:
chemical reaction
reaction analysis
synthesis
chemical structure
structure analysis
article
Drug Descriptors:
***pyridazine derivative**
***benzothiazole derivative**
*benzimidazole derivative
*triazole derivative
hydrazine derivative
semicarbazide derivative
hydrazide derivative
thiophenol derivative
phenylenediamine derivative

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ACCESSION NUMBER: 2005412832 EMBASE Full-text
TITLE: Heterocyclic synthesis with nitriles: Synthesis of some new **thiophene**, **pyridazine**, oxazine, thiopyran, pyrrole, and pyrrolo[1,2-b]pyridazine derivatives.
AUTHOR: Abdelrazek F.M.
CORPORATE SOURCE: F.M. Abdelrazek, Chemistry Department, Faculty of Science, Cairo University, Giza, Egypt. prof_fmrazek@yahoo.com
SOURCE: Synthetic Communications, (2005) Vol. 35, No. 17, pp. 2251-2258. .
Refs: 15
ISSN: 0039-7911 CODEN: SYNCAV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Oct 2005
Last Updated on STN: 13 Oct 2005

ED Entered STN: 13 Oct 2005
Last Updated on STN: 13 Oct 2005

AB 2-Phenyl-1,1,3-tricyanopropene[α-(cyanomethyl)benzylidene- malononitrile] undergoes bromination with N-bromosuccinimide (NBS) to afford 2-phenyl-1,1,3-tricyano-3-bromopropene: [α(bromocyanomethyl)benzylidene malononitrilel. This bromo derivative undergoes reactions with sodium hydrogen sulfide, hydrazine hydrate, phenyl hydrazine, hydroxylamine hydrochloride, ethyl thioglycollate, urea derivatives, and cyanacetohydrazide to afford **thiophene**, 4H-**pyridazines**, 4H-oxazine and 4H-thiopyran, N-substituted pyrrole, and pyrrolof[1,2-b]pyridazine derivatives respectively. Copyright .COPYRGT. Taylor & Francis, Inc.

CT Medical Descriptors:
bromination
synthesis
reaction analysis
proton nuclear magnetic resonance
carbon nuclear magnetic resonance
article
Drug Descriptors:
***thiophene derivative**
***pyridazine derivative**
*oxazine derivative
*thiopyran derivative
*pyrrole derivative
*pyrrolo[1,2 b]pyridazine
nitrile
2 phenyl 1,1,3 tricyanopropene
n bromosuccinimide
2 phenyl 1,1,3 tricyano 3 bromopropene
hydrogen sulfide
hydrazine
phenylhydrazine
hydroxylamine
thioglycolic acid
urea derivative
acetohydrazide
4h pyridazine derivative
4h oxazine derivative
4h thiopyran derivative
unclassified drug
RN (n bromosuccinimide) 128-08-5, 39660-53-2; (hydrogen sulfide) 15035-72-0, 7783-06-4; (hydrazine) 10217-52-4, 13775-80-9, 18500-32-8, 302-01-2, 7803-57-8; (phenylhydrazine) 100-63-0, 59-88-1; (hydroxylamine) 7803-49-8; (thioglycolic acid) 68-11-1; (acetohydrazide) 1068-57-1

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ACCESSION NUMBER: 2003167102 EMBASE Full-text
TITLE: Solid-phase synthesis of heterocycles from 1,4-diketone synthons.
AUTHOR: Raghavan S.; Anuradha K.
CORPORATE SOURCE: S. Raghavan, Organic Division I, Indian Inst. of Chemical Technology, Hyderabad 500 007, India. purush101@yahoo.com
SOURCE: Synlett, (2003) No. 5, pp. 711-713. .
Refs: 21
ISSN: 0936-5214 CODEN: SYNLES
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 May 2003
Last Updated on STN: 19 May 2003
ED Entered STN: 19 May 2003
Last Updated on STN: 19 May 2003
AB The solid-phase synthesis of furans, **thiophenes**, pyrroles and **pyridazines** from 1,4-diketones as the common intermediate is reported. A diverse collection of these heterocyclic compounds is readily prepared in two high yielding steps.
CT Medical Descriptors:
synthesis
chemical reaction

chemical structure
solid
article
Drug Descriptors:
*furan derivative
***thiophene derivative**
*pyrrole derivative
***pyridazine derivative**
*1,4 diketone

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ACCESSION NUMBER: 2002291955 EMBASE Full-text
TITLE: Dramatically enhanced fluorescence of heteroaromatic chromophores upon insertion as spacers into oligo(triacetylene)s.
AUTHOR: Edelmann M.J.; Raimundo J.-M.; Utesch N.F.; Diederich F.; Boudon C.; Gisselbrecht J.-P.; Gross M.
CORPORATE SOURCE: F. Diederich, Laboratorium fur Organische Chemie, ETH-Honggerberg, HCI, CH-8093 Zurich, Switzerland
SOURCE: Helvetica Chimica Acta, (2002) Vol. 85, No. 7, pp. 2195-2213. .
Refs: 44
ISSN: 0018-019X CODEN: HCACAV
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Aug 2002
Last Updated on STN: 29 Aug 2002

ED Entered STN: 29 Aug 2002
Last Updated on STN: 29 Aug 2002

AB In continuation of a previous study on the modulation of π-electron conjugation of oligo(triacetylene)s by insertion of central hetero-spacer fragments between two (E)-hex-3-ene-1,5-diyne ((E)-1,2-diethynylethene, DEE) moieties (Fig. 1), a new series of trimeric hybrid oligomers (14-18 and 22-24, Fig. 2) were prepared (Schemes 1-3). Spacers used were both electron-deficient (quinoxaline-based heterocycles, **pyridazine**) and electron-rich (2,2'-**bithiophene**, 9,9-dioctyl-9H-fluorene) chromophores. With 19-21 (Scheme 4), a series of transition metal complexes was synthesized as potential precursors for nanoscale scaffolding based on both covalent acetylenic coupling and supramolecular assembly. The UV/VIS spectra (Fig. 3) revealed that the majority of spacers provided heterotrimers featuring extended π-electron delocalization. The new hybrid chromophores show a dramatically enhanced fluorescence compared with the DEE dimer 13 and homo-trimer 12 (Fig. 5). This increase in emission intensity appears as a general feature of these systems: even if the spacer molecule is non-fluorescent, the corresponding hetero-trimer may show a strong emission (Table 2). The redox properties of the new hybrid chromophores were determined by cyclic voltammetry (CV) and rotating-disk voltammetry (RDV) (Table 3 and Fig. 5). In each case, the first one-electron reduction step in the hetero-trimers appeared anodically shifted compared with DEE dimer 13 and homo-trimer 12. With larger spacer chromophore extending into two dimensions (as in 14-18, Fig. 2), the anodic shift (by 240-490 mV, Table 3) seems to originate from inductive effects of the two strongly electron-accepting DEE substituents rather than from extended π-electron conjugation along the oligomeric backbone, as had previously been observed for DEE-substituted porphyrins.

CT Medical Descriptors:

*fluorescence
chromatophore
gene insertion
electron
hybridization
synthesis
supramolecular chemistry
ultraviolet spectroscopy
dimerization
oxidation reduction reaction
cyclic potentiometry
article
priority journal
Drug Descriptors:
*oligo(triacetylene) derivative
*acetylene derivative
hex 3 ene 1,5 diyne
1,2 diethynylethene
ethylene derivative
quinoxaline derivative
pyridazine derivative
2,2' bithiophene 9,9 dioctyl 9h fluorene
fluorene derivative
metal complex
porphyrin derivative
unclassified drug

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ACCESSION NUMBER: 96172203 EMBASE Full-text
DOCUMENT NUMBER: 1996172203
TITLE: Amide anions as unexpected activating groups in nucleophilic heteroaromatic substitution.
AUTHOR: Gillies I.; Rees C.W.
CORPORATE SOURCE: Process Research and Development, Glaxo Wellcome Plc, Temple Hill,Dartford, Kent DA1 5AH, United Kingdom
SOURCE: Tetrahedron Letters, (1996) Vol. 37, No. 23, pp. 4065-4068.
ISSN: 0040-4039 CODEN: TELEAY
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 8 Jul 1996
Last Updated on STN: 8 Jul 1996
ED Entered STN: 8 Jul 1996
Last Updated on STN: 8 Jul 1996
AB Nucleophilic displacement of halide by alkoxide in **pyridazines**, phthalazines, a **thiazole** and a thiadiazole is unexpectedly activated by acetamido anion substituents compared to neutral amido and amino substituents.
CT Medical Descriptors:
*drug synthesis
article
reaction analysis
stereochemistry
Drug Descriptors:
pyridazine derivative: AN, drug analysis
pyridazine derivative: DV, drug development

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ACCESSION NUMBER: 94341889 EMBASE Full-text
DOCUMENT NUMBER: 1994341889
TITLE: A new entry to the ethynylation of azaaromatics using bis(tributylstannyl)acetylene in the presence of alkyl chloroformate.
AUTHOR: Itoh T.; Hasegawa H.; Nagata K.; Okada M.; Ohsawa A.
CORPORATE SOURCE: School of Pharmaceutical Sciences, Showa University, 1-5-8 Hatanodai,Shinagawa-ku, Tokyo 142, Japan
SOURCE: Tetrahedron, (1994) Vol. 50, No. 46, pp. 13089-13100. . ISSN: 0040-4020 CODEN: TETRAB
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 7 Dec 1994
Last Updated on STN: 7 Dec 1994

ED Entered STN: 7 Dec 1994
Last Updated on STN: 7 Dec 1994

AB Unstable N-alkoxycarbonyl quaternary salts of azaaromatics were trapped in situ by bis(tributylstannyl)acetylene followed by the treatment with trifluoroacetic acid to give 2-ethynyl adducts in good yields. The same compounds were obtained only in low yields when ethynyltributyltin was used as a nucleophile. The reaction was revealed to be available for various aromatics including pyridine, **pyridazine**, imidazole, **thiazole**, oxazole, and benzodiazines.

CT Medical Descriptors:
*drug synthesis
article
methodology
priority journal
reaction analysis
Drug Descriptors:
*imidazole derivative: AN, drug analysis
*imidazole derivative: DV, drug development
*isoquinoline derivative: AN, drug analysis
*isoquinoline derivative: DV, drug development
*oxazole derivative: AN, drug analysis
*oxazole derivative: DV, drug development
***pyridazine derivative: AN, drug analysis**
***pyridazine derivative: DV, drug development**
*pyridine derivative: DV, drug development
*pyridine derivative: AN, drug analysis
*quinoline derivative: AN, drug analysis
*quinoline derivative: DV, drug development
*quinoxaline derivative: AN, drug analysis
*quinoxaline derivative: DV, drug development
***thiazole derivative: AN, drug analysis**
***thiazole derivative: DV, drug development**

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ACCESSION NUMBER: 95163531 EMBASE Full-text
DOCUMENT NUMBER: 1995163531
TITLE: Heterocyclic synthesis with nitriles: New routes for synthesis of pyridazines, pyridines and their fused derivatives.
AUTHOR: Negm A.M.; Abdelrazek F.M.; Elnagdi M.H.; Shaaban L.H.

CORPORATE SOURCE: Chemistry Department, Faculty of Science, Cairo University,Giza, Egypt
SOURCE: Archives of Pharmacal Research, (1994) Vol. 17, No. 6, pp. 411-414. .
ISSN: 0253-6269 CODEN: APHRDQ
COUNTRY: Korea, Republic of
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 27 Jun 1995
Last Updated on STN: 27 Jun 1995
ED Entered STN: 27 Jun 1995
Last Updated on STN: 27 Jun 1995
AB Phenylazocyanothioacetamide 1 reacts with malononitrile to afford the pyridinethione 4 which reacts with phenacylbromide to yield the pyridine-S-phenacyl derivative 6. 1 reacts with ethyl cyanoacetate to yield the pyridazine derivative, 8, and with phenacyl bromide to afford the N-phenacyl derivative 11, instead of the **thiazole** 10. Compound 11 afforded the pyrazolopyridine 13 on reaction with malononitrile while 10 was obtained on coupling of the **thiazole** 14 with diazotised aniline. Compound 10 reacts with malononitrile to afford the **thiazolyl pyridazine** 15. Compound 1 reacts with malononitrile dimer to afford the pyridopyridazine derivative 17a. 1 reacts also with active methylene heterocycles to afford the pyrazolo and **thiazolo**-fused **pyridazines** 20 and 23 respectively.
CT Medical Descriptors:
*drug synthesis
article
methodology
reaction analysis
Drug Descriptors:
***pyridazine derivative: AN, drug analysis**
***pyridazine derivative: DV, drug development**
*pyridine derivative: DV, drug development
*pyridine derivative: AN, drug analysis
***thiazole derivative: DV, drug development**
***thiazole derivative: AN, drug analysis**
pyrazolo[3,4 c]pyrazole derivative: DV, drug development
pyrazolo[3,4 c]pyrazole derivative: AN, drug analysis
pyrazolo[4,3 b]pyridine derivative: AN, drug analysis
pyrazolo[4,3 b]pyridine derivative: DV, drug development
pyrido[2,3 d]pyridazine derivative: AN, drug analysis
pyrido[2,3 d]pyridazine derivative: DV, drug development
thiazolo[4,5 c]pyridazine derivative: AN, drug analysis
thiazolo[4,5 c]pyridazine derivative: DV, drug development
unclassified drug

L99 ANSWER 63 OF 69 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 94246476 EMBASE Full-text
DOCUMENT NUMBER: 1994246476
TITLE: Hydralazine and other hydrazine derivatives and the formation of DNA adducts.
AUTHOR: Mathison B.H.; Murphy S.E.; Shank R.C.
CORPORATE SOURCE: Environmental Toxicology Program, Community/Environmental Med. Dept., University of California,Irvine, CA 92717, United States
SOURCE: Toxicology and Applied Pharmacology, (1994) Vol. 127, No. 1, pp. 91-98. .
ISSN: 0041-008X CODEN: TXAPA

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 7 Sep 1994
Last Updated on STN: 7 Sep 1994
ED Entered STN: 7 Sep 1994
Last Updated on STN: 7 Sep 1994

AB Previous work has demonstrated that hydrazine after formylation to its corresponding hydrazone may be activated both in vivo and in vitro to a methylating intermediate resulting in the formation of O6-methyl- and N7-methylguanines in DNA. Incubation of calf thymus DNA with the hydrazine derivative, hydralazine, and formaldehyde resulted in the production of N7-methylguanine and two aberrant bases in DNA. These bases were separated by strong cation-exchange high-performance liquid chromatographic fractionation of neutral thermal hydrolysates. Administration of hydralazine to rats resulted in the formation of N7-methylguanine in liver DNA, but the two unknown bases observed in the in vitro experiment could not be demonstrated in vivo. In contrast to hydrazine, administration of hydralazine resulted in the methylation of DNA only at doses approaching the LD50, suggesting that formylation does not represent a significant mechanism for hydralazine toxicity in the system described. Hydralazine in combination with formaldehyde resulted in the formation of triazolophthalazine, a metabolite which has been characterized in man. The ability of 17 other hydrazine derivatives to alkylate liver DNA was determined after single administration to young adult male Sprague-Dawley rats or C57BL6 mice. Quantifiable amounts of N7-methylguanine were measured in liver DNA from animals treated with 10 of the 17 compounds. In 3 of the 10 cases quantifiable amounts of O6-methylguanine were also measured. Methylation of liver DNA guanine was obtained with hydrazine, hydralazine, procarbazine, isoniazid, phenylhydrazine, nialamide, nitrofurazone, maleic hydrazide, **sulfomethoxypyridazine**, and **sulfamethiazole** and two hydrazine-formaldehyde polymerization products, formalazine and tetraformyltrisazine.

CT Medical Descriptors:
*dna adduct
*dna methylation
*drug dna interaction
article
dna alkylation
dose response
Drug Descriptors:
*7 methylguanine
*formaldehyde
*hydralazine
drug metabolite
formalazine
hydrazine
hydrazine derivative
isoniazid
maleic hydrazide
nialamide
nitrofural
phenylhydrazine
procarbazine
sulfamethizole
sulfamethoxypyridazine
tetraformyltrisazine
triazolophthalazine

unclassified drug
RN (7 methylguanine) 578-76-7; (formaldehyde) 50-00-0; (hydralazine) 304-20-1, 86-54-4; (hydrazine) 10217-52-4, 13775-80-9, 18500-32-8, 302-01-2, 7803-57-8; (isoniazid) 54-85-3, 62229-51-0, 65979-32-0; (maleic hydrazide) 123-33-1; (nialamide) 51-12-7; (nitrofural) 59-87-0; (phenylhydrazine) 100-63-0, 59-88-1; (procarbazine) 366-70-1, 671-16-9; (sulfamethizole) 144-82-1; (sulfamethoxypyridazine) 80-35-3
CO Sigma (United States); Aldrich (United States)

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ACCESSION NUMBER: 93203344 EMBASE Full-text
DOCUMENT NUMBER: 1993203344
TITLE: The induction of cytochrome P4502E1 by nitrogen- and sulfur-containing heterocycles: Expression and molecular regulation.
AUTHOR: Sang Geon Kim; Novak R.F.
CORPORATE SOURCE: Institute of Chemical Toxicology, Wayne State University,Detroit, MI 48201, United States
SOURCE: Toxicology and Applied Pharmacology, (1993) Vol. 120, No. 2, pp. 257-265. .
ISSN: 0041-008X CODEN: TXAPA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 15 Aug 1993
Last Updated on STN: 15 Aug 1993
ED Entered STN: 15 Aug 1993
Last Updated on STN: 15 Aug 1993
AB Several structurally related sulfur- and nitrogen-containing heterocycles including **thiazole**, pyrazine, **pyridazine**, pyrimidine, **thiophene**, and triazole, which are present in tobacco, tobacco smoke, and certain foods, have been employed with the goal of characterizing the effects of these agents on the inhibition and expression of P4502E1 in hepatic tissue and on the molecular level regulatory events governing enhanced expression. The results of this study reveal that whereas the binding constants of these compounds to 2E1 moderately correlated with the percentage inhibition of metabolic activity in vitro (r = 0.66), neither inhibition of metabolic activity nor binding to P4502E1 correlated with relative induction of P4502E1 levels (r = 0.07 and 0.03, respectively). **Thiazole**, which produced the greatest inhibition of metabolic activity (88%) and exhibited the highest binding affinity for P4502E1 (35 μM), induced P4502E1 .apprx.fourfold. In contrast, pyrazine and pyridazine, which only marginally inhibited metabolic activity (54 and 41%, respectively), and weakly bound 2E1 (73 and 384 μM, respectively), increased P4502E1 levels .apprx.four- and fivefold, respectively. A common feature associated with these inducers, however, was the substantial decrease in hepatic P4502E1 poly(A)+ RNA levels in treated animals relative to untreated animals. Slot and Northern blot hybridization analyses revealed an .apprx.80% decrease in P4502E1 poly(A)+ RNA levels at 48 hr following treatment of rats with **thiazole**, and at 24 hr following treatment of animals with either pyrazine or pyridazine, relative to controls. P4502E1 poly(A)+ RNA levels appeared to increase gradually, returning to levels which approximated 60% of the P4502E1 poly(A)+ RNA levels present in untreated animals at 48 and 72 hr following treatment with pyrazine or pyridazine, respectively. The results of these experiments show that **thiazole**, pyrazine, and **pyridazine** induce P4502E1 in rats, that the induction of 2E1 is associated with a concomitant decrease

in 2E1 poly(A)+ RNA levels, and that these agents differentially affect the expression of P4502E1.

CT Medical Descriptors:
*enzyme induction
*enzyme inhibition
animal tissue
article
controlled study
male
nonhuman
priority journal
rat
Drug Descriptors:
*cytochrome p450 isoenzyme: EC, endogenous compound
*pyrazine
*pyrazole
***pyridazine**
*pyridine
*pyrimidine
***thiazole**
***thiophene**
*triazole
rna: EC, endogenous compound

RN (pyrazine) 290-37-9; (pyrazole) 288-13-1; (pyridazine) 289-80-5; (pyridine) 110-86-1; (pyrimidine) 289-95-2; (**thiazole**) 288-47-1; (**thiophene**) 110-02-1; (triazole) 37306-44-8; (rna) 63231-63-0

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ACCESSION NUMBER: 92351768 EMBASE Full-text
DOCUMENT NUMBER: 1992351768
TITLE: Condensation of muscimol or thiomuscimol with aminopyridazines yields GABA-A antagonists.
AUTHOR: Melikian A.; Schlewer G.; Chambon J.-P.; Wermuth C.G.
CORPORATE SOURCE: Lab. de Pharmacochimie Moleculaire, Centre de Neurochimie du CNRS, 5, Rue Blaise Pascal,67084 Strasbourg, France
SOURCE: Journal of Medicinal Chemistry, (1992) Vol. 35, No. 22, pp. 4092-4097. .
ISSN: 0022-2623 CODEN: JMCMAR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Dec 1992
Last Updated on STN: 20 Dec 1992

ED Entered STN: 20 Dec 1992
Last Updated on STN: 20 Dec 1992

AB Ten analogs of muscimol and thiomuscimol in which the amino function was delocalized in an amidinic system were prepared by N2 alkylation of 6-aryl-3-**aminopyridazines** with (chloromethyl)isoxazole or (chloromethyl)**isothiazole** derivatives. These muscimol and thiomuscimol derivatives show potent binding properties for GABA-A receptors (they displace [3H]GABA and [3H]gabazine) and provoke convulsions after iv injections. They fit well with the model pharmacophore proposed by our group for the GABA-A antagonists and show similar structure-activity profiles to that of the pyridazinyl-GABAs.

CT Medical Descriptors:
*drug mixture
*drug synthesis

animal experiment
article
convulsion: ET, etiology
drug effect
drug receptor binding
mouse
nonhuman
priority journal
receptor affinity
structure activity relation
Drug Descriptors:
*4 aminobutyric acid a receptor
*4 aminobutyric acid
*muscimol: CB, drug combination
*muscimol: DV, drug development
*muscimol: PD, pharmacology
***pyridazine derivative: CB, drug combination**
***pyridazine derivative: DV, drug development**
***pyridazine derivative: PD, pharmacology**
*thiomuscimol: CB, drug combination
*thiomuscimol: DV, drug development
*thiomuscimol: PD, pharmacology
RN (4 aminobutyric acid) 28805-76-7, 56-12-2; (muscimol) 2763-96-4; (thiomuscimol) 62020-54-6

L99 ANSWER 66 OF 69 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 92285548 EMBASE Full-text
DOCUMENT NUMBER: 1992285548
TITLE: [Heterocycles, LXVIII: Synthesis and reaction of some 2-aryl-5-R-1,2,4-triazolo[2',3':3,2]**thiazolo**[4,5-d]**pyridazines**].
HETEROCYCLEN, 68. MITT.: DARSTELLUNG UND VERHALTEN EINIGER 2-ARYL-5-R-1,2,4-TRIAZOLO[2',3':3,2]-**THIAZOLO**[4,5-D]**PYRIDAZINE.**
AUTHOR: Simiti I.; Zaharia V.; Demian H.
CORPORATE SOURCE: Univ. fur Medizin und Pharmazie, Fakultat fur Pharmazie, Laboratorium fur Organische Chemie, V. Babes-Strasse 41,3400 Cluj-Napoca, Romania
SOURCE: Archiv der Pharmazie, (1992) Vol. 325, No. 9, pp. 609-611.
ISSN: 0365-6233 CODEN: ARPMAS
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: German
ENTRY DATE: Entered STN: 25 Oct 1992
Last Updated on STN: 25 Oct 1992
ED Entered STN: 25 Oct 1992
Last Updated on STN: 25 Oct 1992
CT Medical Descriptors:
*synthesis
article
reaction analysis
Drug Descriptors:
*1,2,4 triazole derivative: AN, drug analysis
*1,2,4 triazole derivative: DV, drug development
***pyridazine derivative: AN, drug analysis**
***pyridazine derivative: DV, drug development**
***thiazole derivative: AN, drug analysis**

***thiazole derivative: DV, drug development**
1,2,4 triazolo[2',3':3,2]thiazolo[4,5 d]pyridazine derivative: AN, drug analysis
1,2,4 triazolo[2',3':3,2]thiazolo[4,5 d]pyridazine derivative: DV, drug development
unclassified drug

L99 ANSWER 67 OF 69 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 80187142 EMBASE Full-text
DOCUMENT NUMBER: 1980187142
TITLE: Studies on cardiovascular agents. VI. Synthesis and coronary vasodilating and antihypertensive activities of 1,2,4-triazolo [1,5-a]pyrimidines fused to heterocyclic systems.
AUTHOR: Sato Y.; Shimoji Y.; Fujita H.; et al.
CORPORATE SOURCE: Cent. Res. Lab., Sankyo Co. Ltd, Tokyo, Japan
SOURCE: Journal of Medicinal Chemistry, (1980) Vol. 23, No. 8, pp. 927-937. .
CODEN: JMCMAR
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Dec 1991
Last Updated on STN: 9 Dec 1991
ED Entered STN: 9 Dec 1991
Last Updated on STN: 9 Dec 1991
AB The synthesis and coronary vasodilating and antihypertensive activities of 1,2,4-trizolo[1,5-a]pyrimidines fused to pyrrole, **thiophene**, pyran, pyridine, and **pyridazine** are described. Among these compounds, 8-tert-butyl-7,8-dihydro-5-methyl-6H-pyrrolo[3,2- e][1,2,4]trizolo[1,5α]pyrimidine was found to be the most promising potential cardiovascular agent, having been shown to be more potent in coronary vasodilating activity than trapidil [7-(diethylamino)-5-methyl- 1,2,4-triazolo[1,5α]pyrimidine] and approximately equipotent to guanethidine sulfate in antihypertensive activity.
CT Medical Descriptors:
*1,2,4 triazolo[1,5 a]pyrimidine derivative
*bumepidil
*blood pressure
*coronary artery dilatation
*dog
*drug analysis
*drug comparison
*drug screening
*drug synthesis
*guinea pig
*heart
*hypertension
*pharmacokinetics
*rat
*structure activity relation
*vasodilatation
mass spectrometry
nuclear magnetic resonance
spontaneously hypertensive rat
ultraviolet spectrophotometry
cardiovascular system

in vitro study
theoretical study
animal experiment
oral drug administration
intravenous drug administration
intraarterial drug administration
Drug Descriptors:
*pyran
***pyridazine**
*pyridine
***thiophene**
guanethidine
trapidil
RN (pyran) 289-66-7, 33941-07-0; (pyridazine) 289-80-5; (pyridine) 110-86-1; (**thiophene**) 110-02-1; (guanethidine) 55-65-2, 60-02-6, 645-43-2; (trapidil) 15421-84-8

L99 ANSWER 68 OF 69 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 78125140 EMBASE Full-text
DOCUMENT NUMBER: 1978125140
TITLE: Chlorophenyl derivatives of pyridazine 3,6 dione.
AUTHOR: Baloniak S.; Mroczkiewicz A.
CORPORATE SOURCE: Zakl. Chem. Org., Inst. Chem. Anal., Akad. Med., Poznan, Poland
SOURCE: Annales Pharmaceutici, (1977) Vol. Vol.12, pp. 65-69. .
CODEN: APMCB4
COUNTRY: Poland
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
LANGUAGE: Polish
SUMMARY LANGUAGE: English
CT Medical Descriptors:
*4 alkoxy 2 (4 chlorophenyl) 2 methylpyridazine 3,6 dione
***6 (3 chlorophenyl) 5 methylpyridazino[4,5 d]thiazolidine**
*bacterium
*drug analysis
*drug identification
*drug screening
*drug synthesis
*microorganism
theoretical study
in vitro study
Drug Descriptors:
***pyridazinone derivative**

L99 ANSWER 69 OF 69 DRUGU COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 1984-35573 DRUGU E Full-text
TITLE: Pharmacological Influence on the Balance of Thromboxane and Prostacyclin in the Organism.
AUTHOR: Lakin K M; Makarov V A; Novikova N V; Tretyak V M; Rukazenkov Y E
LOCATION: Moscow, Russia
SOURCE: Farmakol.Toksikol. (47, No. 2, 67-79, 1984) 220 Ref.
CODEN: FATOAO
AVAIL. OF DOC.: N.A. Semashko Moscow Med. Sci. Inst., Moscow, U.S.S.R.
LANGUAGE: Russian
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB Substances and mechanisms having effects on the balance between thromboxane A2 and prostacyclin are reviewed in relation to their formation and action in the body.

AN 1984-35573 DRUGU E Full-text
E Endocrinology
13 Endocrinology

CT REVIEW *FT

[01] THROMBOXANE-A2 *FT; PROSTACYCLIN *FT; PROSTAGLANDIN-METAB. *FT; BIOSYNTH. *FT; MAIN-TOPIC *FT; PH *FT

[02] THROMBIN *PH; CALCIMYCIN *PH; CYCLOHEXIMIDE *PH; ANGIOTENSIN-2 *PH; OXYTOCIN *PH; AMINAZINE *PH; PROPRANOLOL *PH; CYCLIC-AMP *PH; PAPAVERINE *PH; NICERGOLINE *PH; MEPACRINE *PH; ORGOTEIN *PH; ASPIRIN *PH; INDOMETACIN *PH; PARACETAMOL *PH; IBUPROFEN *PH; VOLTAREN *PH; PHENYLHYDRAZINE *PH; GUAIACOL *PH; NAPROXEN *PH; FLURBIPROFEN *PH; MEFENAMATE *PH; SULINDAC *PH; ESTRADIOL *PH; ADRENALINE *PH; SEROTONIN *PH; UK-80338 *PH; UK-34787 *PH; DAZOXIBEN *PH; BURIMAMIDE *PH; NICOTINATE *PH; OKY-1581 *PH; NICTINDOLE *PH; OKY -1580 *PH; EPL-55712 *PH; N-0164 *PH; TLCK *PH; TOCOPHEROL *PH; HYDRALAZINE *PH; CHLORPROMAZINE *PH; DICLOFENAC *PH; PH *FT

[03] DIPYRIDAMOLE *PH; DIAZOXIDE *PH; NICOTINE *PH; PENTOXIFYLLINE *PH; CLOFIBRATE *PH; PAPAVERINE *PH; NITROGLYCEROL *PH; NITROPRUSSIDE *PH; CLONIDINE *PH; VERAPAMIL *PH; DIHYDRALAZINE *PH; DEFIBROTIDE *PH; FUROSEMIDE *PH; ESTRADIOL *PH; NIFEDIPINE *PH; ASPIRIN *PH; TRAPYMINE *PH; NAFAZATROM *PH; PH *FT

```
=> d que nos 136
L5              STR
L7           21 SEA FILE=REGISTRY SSS FUL L5
L13             STR
L15          85 SEA FILE=REGISTRY SSS FUL L13
L17             QUE  ABB=ON  PLU=ON  EGGENWEILER, H?/AU
L18             QUE  ABB=ON  PLU=ON  WOLF, M?/AU
L19             QUE  ABB=ON  PLU=ON  MERCK/PA,CS,SO
L29           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7
L30          32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15
L31          32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L29 OR L30)
L36           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L31 AND (L17 OR L18 OR L19)


=> d que nos 147
L5              STR
L7           21 SEA FILE=REGISTRY SSS FUL L5
L13             STR
L15          85 SEA FILE=REGISTRY SSS FUL L13
L17             QUE  ABB=ON  PLU=ON  EGGENWEILER, H?/AU
L18             QUE  ABB=ON  PLU=ON  WOLF, M?/AU
L19             QUE  ABB=ON  PLU=ON  MERCK/PA,CS,SO
L44           1 SEA FILE=TOXCENTER ABB=ON  PLU=ON  L7
L45           6 SEA FILE=TOXCENTER ABB=ON  PLU=ON  L15
L46           6 SEA FILE=TOXCENTER ABB=ON  PLU=ON  (L44 OR L45)
L47           1 SEA FILE=TOXCENTER ABB=ON  PLU=ON  L46 AND (L17 OR L18 OR L19)


=> d que nos 162
L13             STR
L17             QUE  ABB=ON  PLU=ON  EGGENWEILER, H?/AU
L18             QUE  ABB=ON  PLU=ON  WOLF, M?/AU
L19             QUE  ABB=ON  PLU=ON  MERCK/PA,CS,SO
L55          35 SEA FILE=WPIX SSS FUL L13
L56          11 SEA FILE=WPIX ABB=ON  PLU=ON  (RACQNP/DCN OR RACVZA/DCN OR
                RACVZB/DCN OR RACVZC/DCN OR RACVZD/DCN OR RACVZE/DCN OR
                RACVZF/DCN OR RACVZG/DCN OR RACVZH/DCN OR RACVZI/DCN OR
                RACVZM/DCN OR RACVZN/DCN OR RACVZO/DCN OR RACVZP/DCN OR
                RACVZ3/DCN OR RACVZ4/DCN OR RACVZ5/DCN OR RACVZ6/DCN OR
                RACVZ7/DCN OR RACVZ8/DCN OR RACVZ9/DCN OR RANV5C/DCN OR
                RANV5G/DCN OR RANV5P/DCN OR RANV5Q/DCN OR RANV6F/DCN OR
                RANV66/DCN OR RA1KDF/DCN OR RA1RZ6/DCN OR RA4W3Q/DCN OR
                RA4XH0/DCN OR RA4X3I/DCN OR RA4X4A/DCN OR RA4X4D/DCN OR
                RA6SZ8/DCN)
L57          11 SEA FILE=WPIX ABB=ON  PLU=ON  L55/DCR
L58          11 SEA FILE=WPIX ABB=ON  PLU=ON  (L56 OR L57)
L59             QUE  ABB=ON  PLU=ON  F530/M0,M1,M2,M3,M4,M5,M6
L61         635 SEA FILE=WPIX ABB=ON  PLU=ON  (L58 OR L59) AND (L17 OR L18 OR
                L19)
L62           1 SEA FILE=WPIX ABB=ON  PLU=ON  L61 AND L58


=> d que 172
L17             QUE  ABB=ON  PLU=ON  EGGENWEILER, H?/AU
L18             QUE  ABB=ON  PLU=ON  WOLF, M?/AU
L19             QUE  ABB=ON  PLU=ON  MERCK/PA,CS,SO
L28             QUE  ABB=ON  PLU=ON  ?THIAZOL? OR ?THIOPHEN?
```

```
L65             QUE  ABB=ON  PLU=ON  PYRIDAZINES+PFT,OLD,NEW,NT/CT
L66             QUE  ABB=ON  PLU=ON  THIOPHENES+PFT,OLD,NEW,NT/CT
L67             QUE  ABB=ON  PLU=ON  THIAZOLES+PFT,OLD,NEW,NT/CT
L68         257 SEA FILE=MEDLINE ABB=ON  PLU=ON  L65 AND (L66 OR L67 OR L28)
L72           2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L68 AND (L17 OR L18 OR L19)


=> d que l88
L17             QUE  ABB=ON  PLU=ON  EGGENWEILER, H?/AU
L18             QUE  ABB=ON  PLU=ON  WOLF, M?/AU
L19             QUE  ABB=ON  PLU=ON  MERCK/PA,CS,SO
L28             QUE  ABB=ON  PLU=ON  ?THIAZOL? OR ?THIOPHEN?
L73             QUE  ABB=ON  PLU=ON  "PYRIDAZINE DERIVATIVE"+PFT,OLD,NEW,
                NT/CT
L74             QUE  ABB=ON  PLU=ON  "PYRIDAZINONE DERIVATIVE"+PFT,OLD,NE
                W,NT/CT
L75             QUE  ABB=ON  PLU=ON  "THIAZOLE DERIVATIVE"+PFT,OLD,NEW,NT
                /CT
L76             QUE  ABB=ON  PLU=ON  "THIOPHENE DERIVATIVE"+PFT,OLD,NEW,N
                T/CT
L77         217 SEA FILE=EMBASE ABB=ON  PLU=ON  (L73 OR L74) AND ((L75 OR L76)
                OR L28)
L88           3 SEA FILE=EMBASE ABB=ON  PLU=ON  L77 AND (L17 OR L18 OR L19)


=> d his l93

     (FILE 'BIOSIS, PASCAL, JICST-EPLUS, JAPIO, LIFESCI, BIOENG, BIOTECHNO,
     BIOTECHDS, DRUGU, DRUGB, VETU, VETB, SCISEARCH, CONFSCI, DISSABS' ENTERED
     AT 12:26:38 ON 20 DEC 2006)
L93             1 S L91 AND L19-L20

=> d que l93
L19             QUE  ABB=ON  PLU=ON  MERCK/PA,CS,SO
L20             QUE  ABB=ON  PLU=ON  (WOLF OR EGGENWEILER)/AU
L27             QUE  ABB=ON  PLU=ON  ?PYRIDAZIN?
L28             QUE  ABB=ON  PLU=ON  ?THIAZOL? OR ?THIOPHEN?
L91         423 SEA L27(7A) L28
L93           1 SEA L91 AND (L19 OR L20)


=> dup rem l36 l47 l62 l72 l88 l93
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PROCESSING COMPLETED FOR L36
PROCESSING COMPLETED FOR L47
PROCESSING COMPLETED FOR L62
PROCESSING COMPLETED FOR L72
PROCESSING COMPLETED FOR L88
PROCESSING COMPLETED FOR L93
L100          9 DUP REM L36 L47 L62 L72 L88 L93 (2 DUPLICATES REMOVED)
                ANSWERS '1-3' FROM FILE HCAPLUS
                ANSWERS '4-5' FROM FILE MEDLINE
                ANSWERS '6-8' FROM FILE EMBASE
                ANSWER '9' FROM FILE BIOSIS

=> file stnguide
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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Dec 19, 2006 (20061219/UP).

=> d ibib ed ab 1-9
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, MEDLINE, EMBASE, BIOSIS' - CONTINUE?
(Y)/N:y



L100 ANSWER 1 OF 9  HCAPLUS  COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2004:2882  HCAPLUS  Full-text
DOCUMENT NUMBER:          140:77154
TITLE:                    Preparation of thiazoles as phosphodiesterase IV
                          inhibitors for the treatment of osteoporosis, tumors
                          and cachexia
INVENTOR(S):              Egggenweiler, Hans-Michael; Wolf, Michael
PATENT ASSIGNEE(S):       Merck Patent G.m.b.H., Germany
SOURCE:                   PCT Int. Appl., 125 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2004000839         A1    20031231    WO 2003-EP4434          20030428
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     DE 10227269           A1    20040108    DE 2002-10227269        20020619
     CA 2489902            A1    20031231    CA 2003-2489902         20030428
     AU 2003232215         A1    20040106    AU 2003-232215          20030428
     BR 2003011879         A     20050315    BR 2003-11879           20030428
     EP 1513837            A1    20050316    EP 2003-760583          20030428
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EP 1513837 B1 20060830
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
CN 1662529 A 20050831 CN 2003-814060 20030428
JP 2005530825 T 20051013 JP 2004-514623 20030428
AT 338041 T 20060915 AT 2003-760583 20030428
US 2005222160 A1 20051006 US 2004-518503 20041220
PRIORITY APPLN. INFO.: DE 2002-10227269 A 20020619
WO 2003-EP4434 W 20030428

OTHER SOURCE(S): MARPAT 140:77154
ED Entered STN: 02 Jan 2004
AB Title compds. I [R1, R2 = H, OH, OR8, etc.; R8 = A, cycloalkyl, alkenyl, etc.; R3 = H, A"R7, COA"R7, etc.; A = alkyl, alkenyl; R7 = H, CO2H, CONH2, etc.; A" = alkylene, alkenylene, cycloalkylene, etc.; V, W = O, OH with the proviso that if V = O, then W = H, H; B = (un)substituted aromatic isocyclic, heterocyclic e.g., pyridyl, pyridyl-N- oxide, thienyl, etc.; X = N, CR3] their pharmaceutically acceptable salts and formulations were prepared For example, coupling of acid chloride II, e.g., prepared from 4-methyl-2-pyridin-2-ylthiazole-5-carboxylic acid Me ester in 3-steps, and 3-(3-cyclopentyloxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazine afforded claimed thiazole III. Compds. I are claimed useful as phosphodiesterase IV inhibitors (no data provided) for the treatment of osteoporosis, tumors, cachexia, etc.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L100 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:189365 HCAPLUS Full-text
DOCUMENT NUMBER: 139:78424
TITLE: Pyridazinones as selective cyclooxygenase-2 inhibitors
AUTHOR(S): Li, Chun Sing; Brideau, Christine; Chan, Chi Chung; Savoie, Chantal; Claveau, David; Charleson, Stella; Gordon, Robert; Greig, Gillian; Gauthier, Jacques Yves; Lau, Cheuk K.; Riendeau, Denis; Therien, Michel; Wong, Elizabeth; Prasit, Petpiboon
CORPORATE SOURCE: **Merck** Frosst Centre for Therapeutic Research, Pointe-Claire-Dorval, QC, 1005, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(4), 597-600
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:78424
ED Entered STN: 11 Mar 2003
AB Pyridazinone was found to be an excellent core template for selective COX-2 inhibitors. Two potent, selective and orally active COX-2 inhibitors (I and II), which were highly efficacious in rat paw edema and rat pyresis models, have been obtained.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L100 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:635750 HCAPLUS Full-text
DOCUMENT NUMBER: 129:275920
TITLE: Preparation of pyridazinones as inhibitors of cyclooxygenase-2
INVENTOR(S): Li, Chun Sing; Prasit, Petpiboon; Gauthier, Jacques Y.; Lau, Cheuk K.; Therien, Michel
PATENT ASSIGNEE(S): **Merck** Frosst Canada Inc., Can.
SOURCE: PCT Int. Appl., 87 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9841511	A1	19980924	WO 1998-CA233		19980312
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2283399	A1	19980924	CA 1998-2283399		19980312
CA 2283399	C	20060221			
AU 9864913	A	19981012	AU 1998-64913		19980312
AU 738727	B2	20010927			
EP 975604	A1	20000202	EP 1998-910544		19980312
EP 975604	B1	20040721			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
JP 2001514669	T	20010911	JP 1998-539982		19980312
AT 271547	T	20040815	AT 1998-910544		19980312
ES 2224366	T3	20050301	ES 1998-910544		19980312
US 6004960	A	19991221	US 1998-42174		19980313
PRIORITY APPLN. INFO.:			US 1997-40791P	P	19970314
			GB 1997-7487	A	19970414
			WO 1998-CA233	W	19980312

OTHER SOURCE(S): MARPAT 129:275920
ED Entered STN: 08 Oct 1998
AB The title compds. [I; X = a bond, (CH2)m (m = 1-2); CO, etc.; R1 = Me, NH2. NHC(O)CF3; R2 = (CR6R7)nR8 (R6, R7 = H, C1-10 alkyl, C1-10 fluoroalkyl; R8 = C1-10 alkyl, (un)substituted Ph, naphthyl, etc.); R3 = C1-10 alkyl, (un)substituted Ph, naphthyl, etc.; R4 = H, halo, C1-6 alkyl], useful in treating an inflammatory disease susceptible to treatment with a non-steroidal antiinflammatory agent, and cyclooxygenase-2 mediated diseases, were prepared Thus, reaction of 5-hydroxy-4-(4-methylsulfonyl)phenyl-3-phenyl-5H-furan-2-one with phenylhydrazine in EtOH afforded 30% I [X = a bond; R1 = Me; R2 = Ph; R3 = Ph; R4 = H] which showed IC50 of 0.08 against COX-2 using CHO cell line assay.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L100 ANSWER 4 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2000202347 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10737739
TITLE: Molecular modeling of the aldose reductase-inhibitor complex based on the X-ray crystal structure and studies with single-site-directed mutants.
AUTHOR: Singh S B; Malamas M S; Hohman T C; Nilakantan R; Carper D A; Kitchen D
CORPORATE SOURCE: Wyeth Ayerst Research, CN 8000, Princeton, New Jersey 08543-8000, National Eye Institute, NIH, Bethesda, Maryland 20892, USA.. **suresh singh@merck.com**
SOURCE: Journal of medicinal chemistry, (2000 Mar 23) Vol. 43, No. 6, pp. 1062-70.
Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 21 Apr 2000
Last Updated on STN: 21 Apr 2000
Entered Medline: 13 Apr 2000

ED Entered STN: 21 Apr 2000
Last Updated on STN: 21 Apr 2000
Entered Medline: 13 Apr 2000

AB Aldose reductase (AR) has been implicated in the etiology of the secondary complications of diabetes. This enzyme catalyzes the reduction of glucose to sorbitol using nicotinamide adenine dinucleotide phosphate as an essential cofactor. AR has been localized at the sites of tissue damage, and inhibitors of this enzyme prevent the development of neuropathy, nephropathy, retinopathy, and cataract formation in animal models of diabetes. The crystal structure of AR complexed with zopolrestat, a potent inhibitor of AR, has been described.(1) We have generated a model of the AR-inhibitor complex based on the reported Calpha coordinates of the protein and results of a structure-activity relationship study using four structurally distinct classes of inhibitors, recombinant human AR, and four single-site-directed mutants of this enzyme. The effects of the site-directed mutations on residues within the active site of the enzyme were evaluated by average interaction energy calculations and by calculations of carbon atom surface area changes. These values correlated well with the IC(50) values for zopolrestat with the wild-type and mutant enzymes, validating the model. On the basis of the zopolrestat-binding model, we have proposed binding models for 10 other AR inhibitors. Our models have enabled us to gain a qualitative understanding of the binding domains of the enzyme and how different inhibitors impact the size and shape of the binding site.

L100 ANSWER 5 OF 9 MEDLINE on STN
ACCESSION NUMBER: 1999083918 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9866686
TITLE: Analysis of prostaglandin G/H synthase-2 inhibition using peroxidase-induced luminol luminescence.
AUTHOR: Forghani F; Ouellet M; Keen S; Percival M D; Tagari P
CORPORATE SOURCE: **Merck** Frosst Centre for Therapeutic Research, Pointe Claire-Dorval, Quebec, Canada.
SOURCE: Analytical biochemistry, (1998 Nov 15) Vol. 264, No. 2, pp. 216-21.
Journal code: 0370535. ISSN: 0003-2697.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 1 Mar 1999
Last Updated on STN: 1 Mar 1999
Entered Medline: 12 Feb 1999

ED Entered STN: 1 Mar 1999
Last Updated on STN: 1 Mar 1999
Entered Medline: 12 Feb 1999

AB The inducible form of the heme-protein prostaglandin G/H synthase (PGHS-2 or COX-2) has been established as a pivotal enzyme in the cascade of events leading to inflammation, hyperalgesia, and pyresis and represents a major therapeutic target in inflammatory disease. Accordingly, we have exploited the heme-catalyzed hydroperoxidase activity of recombinant hCOX-2 to generate luminescence in the presence of luminol, or a cyclic naphthalene hydrazide,

and the substrate arachidonic acid. Arachidonate-induced luminescence was shown to be an index of real-time catalytic activity and demonstrated the turnover inactivation of the enzyme. Luminol luminescence was proportional to hCOX-2 concentration and gave accurate Km determinations for arachidonate. Inhibition of hCOX-2 activity, measured by luminescence, by a variety of selective (for COX-2) and nonselective inhibitors showed rank orders of potency similar to those observed with other in vitro and whole cell methods using the recombinant protein. The sensitivity of the luminescence assay also allowed determination of inhibitor potency at substrate concentrations below Km, distinguishing competitive inhibitors such as ibuprofen from time-dependent inhibitors such as DuP-697. Finally the use of higher quantum-yielding luminol analogues allowed measurement of cyclooxygenase activity at extremely low substrate and protein concentrations, enabling a variety of novel assay formats.

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ACCESSION NUMBER: 2005536242 EMBASE Full-text
TITLE: Mild and practical method for the α-arylation of nitriles with heteroaryl halides.
AUTHOR: Klapars A.; Waldman J.H.; Campos K.R.; Jensen M.S.; McLaughlin M.; Chung J.Y.L.; Cvetovich R.J.; Chen C.-Y.
CORPORATE SOURCE: A. Klapars, Department of Process Research, **Merck** Research Laboratories, P.O. Box 2000, Rahway, NJ 07065, United States. artis_klapars@**merck**.com
SOURCE: Journal of Organic Chemistry, (25 Nov 2005) Vol. 70, No. 24, pp. 10186-10189. .
Refs: 22
ISSN: 0022-3263 CODEN: JOCEAH
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Dec 2005
Last Updated on STN: 29 Dec 2005
ED Entered STN: 29 Dec 2005
Last Updated on STN: 29 Dec 2005

AB A mild and transition-metal-free method for theα-arylation of a liphatic nitriles with activated heteroaryl halides was developed using NaHMDS o r KHMDS as base at ambient temperature. The key to the success of this method is generation of the nitrile anion in the presence of the heteroaryl halide. The method is applicable to both primary and secondary carbonitriles and a wide range of heteroaryl halides. Selective monoarylation was observed with primary carbonitriles. The operational simplicity and the mild reaction conditions add to the value of this methodas a practical alternative to the preparation of α-heteroaryl carbonitriles. .COPYRGT. 2005 American Chemical Society.

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ACCESSION NUMBER: 2005504604 EMBASE Full-text
TITLE: P38 MAP kinase inhibitors: Evolution of imidazole-based and pyrido-pyrimidin-2-one lead classes.
AUTHOR: Natarajan S.R.; Doherty J.B.
CORPORATE SOURCE: S.R. Natarajan, Department of Medicinal Chemistry, **Merck** Research Laboratories, P.O. Box 2000, Rahway,

NJ 07065, United States. ravi_natarajan@merck.com
SOURCE: Current Topics in Medicinal Chemistry, (2005) Vol. 5, No. 10, pp. 987-1003. .
Refs: 25
ISSN: 1568-0266 CODEN: CTMCCL
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 28 Nov 2005
Last Updated on STN: 28 Nov 2005
ED Entered STN: 28 Nov 2005
Last Updated on STN: 28 Nov 2005
AB The initial disclosure of tri-substituted imidazole-based drug molecules such as 1 for inhibition of p38 MAP kinase by SmithKline Beecham (SB) sparked an effort in this area at Merck and other pharmaceutical research establishments. Although analogs in this class have shown good inhibitory properties against p38 MAP kinase, their selectivity profile were modest and left much room for improvement. Attempts to discover newer compounds with improved selectivity over the prototypical SB compound 203580 (1), led to the discovery of a new sub-class of p38 inhibitors typified by compound 18 at Merck. Although this benchmark compound was potent, highly selective and orally efficacious it was burdened with compound related adverse effects in dogs that has delayed further development. In 1999, a new class of p38 inhibitors represented by clinical candidate VX-745 (26), was disclosed by Vertex Pharmaceuticals. This compound displayed unprecedented selectivity due to its unique mode of binding to the active site in p38 MAP kinase. Inspired by the exquisite selectivity profile of VX-745 [26] a scaffold re-design was initiated at Merck which resulted in the discovery of the quinazolinone, pyrimido-pyrimidone, pyrido-pyrimidone, quinolinone and naphthyridinone based p38 inhibitors. .COPYRGT. 2005 Bentham Science Publishers Ltd.

L100 ANSWER 8 OF 9 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2002293083 EMBASE Full-text
TITLE: Pharmacological characterization of a novel cell line expressing human α(4)β(3)δ GABA(A) receptors.
AUTHOR: Brown N.; Kerby J.; Bonnert T.P.; Whiting P.J.; Wafford K.A.
CORPORATE SOURCE: K.A. Wafford, Merck Sharp and Dohme Res. Lab., Neuroscience Research Centre, Eastwick Road, Harlow, Essex CM20 2QR, United Kingdom. keith_wafford@merck.com
SOURCE: British Journal of Pharmacology, (2002) Vol. 136, No. 7, pp. 965-974. .
Refs: 38
ISSN: 0007-1188 CODEN: BJPCBM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 5 Sep 2002

Last Updated on STN: 5 Sep 2002

ED Entered STN: 5 Sep 2002
Last Updated on STN: 5 Sep 2002

AB 1. The pharmacology of the stable cell line expressing human α(4)β(3)δ GABA(A) receptor was investigated using whole-cell patch-clamp techniques. 2. α(4)β(3)δ receptors exhibited increased sensitivity to GABA when compared to α(4)β(3)γ(2) receptors, with EC(50)'s of 0.50 (0.46, 0.53) μM and 2.6 (2.5, 2.6) μM respectively. Additionally, the GABA partial agonists piperidine-4-sulphonate (P4S) and 4,5,6,7- **tetrahydroisothiazolo**-[5,4-c]pyridin-3-ol (THIP) displayed markedly higher efficacy at α(4)β(3)δ receptors, indeed THIP demonstrated greater efficacy than GABA at these receptors. 3. The δ subunit conferred slow desensitization to GABA, with rate constants of 4.8 ± 0.5 s for α(4)β(3)δ and 2.5 ± 0.2 s for α(4)β(3)γ(2). However, both P4S and THIP demonstrated similar levels of desensitization on both receptor subtypes suggesting this effect is agonist specific. 4. α(4)β(3)δ and α(4)β(3)γ(2) demonstrated equal sensitivity to inhibition by the cation zinc (2-3 μM IC(50)). However, α(4)β(3)δ receptors demonstrated greater sensitivity to inhibition by lanthanum. The IC(50) for GABA antagonists SR-95531 and picrotoxin, was similar for α(4)β(3)δ and α(4)β(3)γ(2). Likewise, inhibition was observed on both subtypes at high and low pH. 5. α(4)β(3)δ receptors were insensitive to modulation by benzodiazepine ligands. In contrast Ro15-4513 and bretazenil potentiated GABA responses on α(4)β(3)γ(2) cells, and the inverse agonist DMCM showed allosteric inhibition of α(4)β(3)γ(2) receptors. 6. The efficacy of neurosteroids at α(4)β(3)δ receptors was greatly enhanced over that observed at α(4)β(3)γ(2) receptors. The greatest effect was observed using THDOC with 524 ± 71.6% potentiation at α(4)β(3)δ and 297.9 ± 49.7% at α(4)β(3)γ(2) receptors. Inhibition by the steroid pregnenolone sulphate however, showed no subtype selectivity. The efficacy of both pentobarbitone and propofol was slightly augmented and etomidate greatly enhanced at α(4)β(3)δ receptors versus α(4)β(3)γ(2) receptors. 7. We show that the α(4)β(3)δ receptor has a distinct pharmacology and kinetic profile. With its restricted distribution within the brain and unique pharmacology this receptor may play an important role in the action of neurosteroids and anaesthetics.

L100 ANSWER 9 OF 9 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1989:185257 BIOSIS Full-text
DOCUMENT NUMBER: PREV198987096523; BA87:96523
TITLE: SYNTHESIS OF THYROID HORMONE ANALOGUES PART 1. PREPARATION OF 3' HETEROARYLMETHYL-3 5-DIIODO-L-THYRONINES VIA PHENOL-DINITROPHENOL CONDENSATION AND RELATIONSHIPS BETWEEN STRUCTURE AND SELECTIVE THYROMIMETIC ACTIVITY.
AUTHOR(S): LEESON P D [Reprint author]; EMMETT J C
CORPORATE SOURCE: **MERCK** SHARP DOHME RES LAB, NEUROSCI RES CENT, TERLINGS PARK, EASTWICK ROAD, HARLOW, ESSEX, CM20 2QR, UK
SOURCE: Journal of the Chemical Society Perkin Transactions I, (1988) No. 12, pp. 3085-3096.
CODEN: JCPRB4. ISSN: 0300-922X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 9 Apr 1989
Last Updated on STN: 20 Jun 1989

ED Entered STN: 9 Apr 1989
Last Updated on STN: 20 Jun 1989

AB 3'-Heteroarylmethyl analogues (1)-(8) of the natural thyroid hormone 3,3'5-tri-iodo-L-thyronine (T3) were synthesized as potential selective (cardiac-sparing) thyromimetics. The diphenyl ether moiety was constructed by condensation of 3-substituted 4-methoxyphenols with a 3,5-dinitro-L-tyrosine derivative. Synthesis of the key phenols (28)-(32) required the in situ preparation, at low temperatures, of the novel metallated species 2-lithio-5-methoxypyridine (14), 5-lithio-2- methoxypyrimidine (15), 5-lithio-2-methylpyridine (16), 5-bromo-4-lithio-2-methoxypyridine (18), and 2,6-difluoro-3-lithiopyridine (19), followed by reaction with the benzaldehyde (20). Alternative routes to the **pyridazinone** (36) and **thiazolone** (37) phenols were developed from the benzyl bromide (33). Structure-activity relationships indicate that selective thyromimetic activity is associated with 2-oxyheteroaren-5-ylmethyl 3'-substitution, as found in the pyridone (1), **pyridazinone** (2), hydroxypyridine (4) and **thiazolone** (8). The location of the oxy substituent in the heterocycle is critical for both hormonal activity and for binding to the T3 receptor.

=> file stnguide
FILE 'STNGUIDE' ENTERED AT 12:51:32 ON 20 DEC 2006
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Dec 19, 2006 (20061219/UP).

=> d his ful

(FILE 'HOME' ENTERED AT 11:10:44 ON 20 DEC 2006)

FILE 'ZCAPLUS' ENTERED AT 11:11:04 ON 20 DEC 2006
E US2004-518503/APPS

FILE 'HCAPLUS' ENTERED AT 11:12:26 ON 20 DEC 2006
L1 1 SEA ABB=ON PLU=ON US2004-518503/APPS
SAVE TEMP L1 JAI503HCAAPP/A

FILE 'STNGUIDE' ENTERED AT 11:12:57 ON 20 DEC 2006
D QUE

FILE 'HCAPLUS' ENTERED AT 11:13:35 ON 20 DEC 2006
D IBIB ED AB IND

FILE 'STNGUIDE' ENTERED AT 11:13:41 ON 20 DEC 2006

FILE 'WPIX' ENTERED AT 11:14:28 ON 20 DEC 2006
L2 1 SEA ABB=ON PLU=ON US2004-518503/APPS
SAVE TEMP L2 JAI503WPIAPP/A

FILE 'STNGUIDE' ENTERED AT 11:14:52 ON 20 DEC 2006
D QUE

FILE 'WPIX' ENTERED AT 11:15:06 ON 20 DEC 2006
D IALL CODE L2

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     FILE 'HCAPLUS' ENTERED AT 11:16:10 ON 20 DEC 2006
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               SAVE TEMP L4 JAI503REGAPP/A
               D SCAN

     FILE 'STNGUIDE' ENTERED AT 11:16:52 ON 20 DEC 2006

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L5             STR

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L6            1 SEA SSS SAM L5
               D SCAN

     FILE 'STNGUIDE' ENTERED AT 11:22:09 ON 20 DEC 2006
               D QUE STAT

     FILE 'REGISTRY' ENTERED AT 11:23:52 ON 20 DEC 2006
               D QUE STAT
L7           21 SEA SSS FUL L5
               SAVE TEMP L7 JAI503PSET1/A
L8             ANALYZE PLU=ON  L7 1- LC :        4 TERMS
               D 1-

     FILE 'LREGISTRY' ENTERED AT 11:25:10 ON 20 DEC 2006
L9             STR L5

     FILE 'REGISTRY' ENTERED AT 11:25:45 ON 20 DEC 2006
L10            1 SEA SSS SAM L9
               D QUE STAT

     FILE 'STNGUIDE' ENTERED AT 11:26:51 ON 20 DEC 2006

     FILE 'LREGISTRY' ENTERED AT 11:34:30 ON 20 DEC 2006
L11            STR L9

     FILE 'REGISTRY' ENTERED AT 11:35:45 ON 20 DEC 2006
L12          35 SEA SSS SAM L11

     FILE 'LREGISTRY' ENTERED AT 11:36:15 ON 20 DEC 2006
L13            STR L11

     FILE 'REGISTRY' ENTERED AT 11:36:48 ON 20 DEC 2006
L14            4 SEA SSS SAM L13
               D SCAN
               D QUE STAT
L15          85 SEA SSS FUL L13
               SAVE TEMP L15 JAI503PSET2/A
L16            ANALYZE PLU=ON  L15 1- LC :        7 TERMS
               D 1-

     FILE 'STNGUIDE' ENTERED AT 11:39:33 ON 20 DEC 2006

     FILE 'ZCAPLUS' ENTERED AT 11:40:35 ON 20 DEC 2006
L17            QUE ABB=ON  PLU=ON  EGGENWEILER, H?/AU
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L18             QUE ABB=ON  PLU=ON  WOLF, M?/AU
L19             QUE ABB=ON  PLU=ON  MERCK/PA,CS,SO
L20             QUE ABB=ON  PLU=ON  (WOLF OR EGGENWEILER)/AU
L21             QUE ABB=ON  PLU=ON  AY<2004 OR PY<2004 OR PRY<2004 OR MY<2004
                OR REVIEW/DT
L22             QUE ABB=ON  PLU=ON  AY<2004 OR PY<2004 OR PRY<2004

     FILE 'REGISTRY' ENTERED AT 11:42:50 ON 20 DEC 2006
L23           3 SEA ABB=ON  PLU=ON  L15 AND CASREACT/LC

     FILE 'STNGUIDE' ENTERED AT 11:43:06 ON 20 DEC 2006

     FILE 'ZCAPLUS' ENTERED AT 11:43:35 ON 20 DEC 2006
L24             QUE ABB=ON  PLU=ON  ?PHOSPHODIESTERAS? OR (?PHOSPHO(W)DIESTERAS
                ?) OR (?PHOSPHODI(W)ESTERAS?)

     FILE 'REGISTRY' ENTERED AT 11:44:37 ON 20 DEC 2006
L25          14 SEA ABB=ON  PLU=ON  L4 NOT L15
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 11:44:55 ON 20 DEC 2006

     FILE 'REGISTRY' ENTERED AT 11:46:06 ON 20 DEC 2006
L26          21 SEA ABB=ON  PLU=ON  L15 AND L4

     FILE 'STNGUIDE' ENTERED AT 11:46:35 ON 20 DEC 2006

     FILE 'ZCAPLUS' ENTERED AT 11:46:38 ON 20 DEC 2006
L27             QUE ABB=ON  PLU=ON  ?PYRIDAZIN?
L28             QUE ABB=ON  PLU=ON  ?THIAZOL? OR ?THIOPHEN?
                D SAVED

     FILE 'HCAPLUS' ENTERED AT 11:49:00 ON 20 DEC 2006
L29           1 SEA ABB=ON  PLU=ON  L7
L30          32 SEA ABB=ON  PLU=ON  L15
L31          32 SEA ABB=ON  PLU=ON  (L29 OR L30)
L32          31 SEA ABB=ON  PLU=ON  L31 AND (L24 OR L27 OR L28)
L33          32 SEA ABB=ON  PLU=ON  L31 OR L32
L34          31 SEA ABB=ON  PLU=ON  L33 AND L21
L35          32 SEA ABB=ON  PLU=ON  (L33 OR L34)
                SAVE TEMP L35 JAI503HCAB/A
L36           3 SEA ABB=ON  PLU=ON  L31 AND (L17 OR L18 OR L19)
                D SCAN TI HIT
                SAVE TEMP L36 JAI503HCAINV/A

     FILE 'USPATFULL, USPAT2' ENTERED AT 11:51:32 ON 20 DEC 2006
L37           1 SEA ABB=ON  PLU=ON  L7
L38          42 SEA ABB=ON  PLU=ON  L15
L39          42 SEA ABB=ON  PLU=ON  (L37 OR L38)
L40           1 SEA ABB=ON  PLU=ON  L39 AND L24/TI,IT,CC,CT,ST,STP,BI,AB
L41          36 SEA ABB=ON  PLU=ON  L39 AND A61?/IPC
L42           1 SEA ABB=ON  PLU=ON  L41 AND A61P?/IPC
L43           2 SEA ABB=ON  PLU=ON  L37 OR L40 OR L42
                SAVE TEMP L43 JAI503USP1B/A
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 11:54:12 ON 20 DEC 2006

     FILE 'TOXCENTER' ENTERED AT 11:54:29 ON 20 DEC 2006
L44           1 SEA ABB=ON  PLU=ON  L7
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L45             6 SEA ABB=ON  PLU=ON  L15
L46             6 SEA ABB=ON  PLU=ON  (L44 OR L45)
                  SAVE TEMP L46 JAI503TOXB/A
L47             1 SEA ABB=ON  PLU=ON  L46 AND (L17 OR L18 OR L19)
                  SAVE TEMP L47 JAI503TOXINV/A

     FILE 'CASREACT' ENTERED AT 11:55:28 ON 20 DEC 2006
L48             3 SEA ABB=ON  PLU=ON  L23
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     FILE 'STNGUIDE' ENTERED AT 11:56:11 ON 20 DEC 2006
                  D SAVED

     FILE 'BEILSTEIN' ENTERED AT 11:56:55 ON 20 DEC 2006
                  D QUE L15
L49            17 SEA SSS FUL L13
                  SAVE TEMP L49 JAI503BEIP/A
L50             1 SEA ABB=ON  PLU=ON  L49 NOT BABSAN/FA
                  SELECT L49 1- BABSAN

     FILE 'BABS' ENTERED AT 11:58:18 ON 20 DEC 2006
L51             6 SEA ABB=ON  PLU=ON  (5596494/AN OR 6388164/AN OR 5856247/AN OR
                  6347066/AN OR 6428743/AN OR 6531693/AN)
                  SAVE TEMP L51 JAI503BAB/A

     FILE 'CHEMINFORMRX' ENTERED AT 11:58:59 ON 20 DEC 2006
                  D QUE L15
L52             0 SEA SSS SAM L13 (      0 REACTIONS)
L53             2 SEA SSS FUL L13 (      6 REACTIONS)
                  SAVE TEMP L53 JAI503CHMP/A
                  D SCAN

     FILE 'STNGUIDE' ENTERED AT 12:00:07 ON 20 DEC 2006
                  D SAVED

     FILE 'WPIX' ENTERED AT 12:00:45 ON 20 DEC 2006
                  D QUE L15
L54             2 SEA SSS SAM L13
L55            35 SEA SSS FUL L13
                  SAVE TEMP L55 JAI503WPIS/A
                  SELECT L55 1- SDCN
L56            11 SEA ABB=ON  PLU=ON  (RACQNP/DCN OR RACVZA/DCN OR RACVZB/DCN OR
                  RACVZC/DCN OR RACVZD/DCN OR RACVZE/DCN OR RACVZF/DCN OR
                  RACVZG/DCN OR RACVZH/DCN OR RACVZI/DCN OR RACVZM/DCN OR
                  RACVZN/DCN OR RACVZO/DCN OR RACVZP/DCN OR RACVZ3/DCN OR
                  RACVZ4/DCN OR RACVZ5/DCN OR RACVZ6/DCN OR RACVZ7/DCN OR
                  RACVZ8/DCN OR RACVZ9/DCN OR RANV5C/DCN OR RANV5G/DCN OR
                  RANV5P/DCN OR RANV5Q/DCN OR RANV6F/DCN OR RANV66/DCN OR
                  RA1KDF/DCN OR RA1RZ6/DCN OR RA4W3Q/DCN OR RA4XH0/DCN OR
                  RA4X3I/DCN OR RA4X4A/DCN OR RA4X4D/DCN OR RA6SZ8/DCN)
L57            11 SEA ABB=ON  PLU=ON  L55/DCR
L58            11 SEA ABB=ON  PLU=ON  (L56 OR L57)
                  SAVE TEMP L58 JAI503WPIB/A
L59               QUE ABB=ON  PLU=ON  F530/M0,M1,M2,M3,M4,M5,M6
L60             4 SEA ABB=ON  PLU=ON  L58 NOT L59
                  D TRI 1-4
L61           635 SEA ABB=ON  PLU=ON  (L58 OR L59) AND (L17 OR L18 OR L19)
L62             1 SEA ABB=ON  PLU=ON  L61 AND L58
                  SAVE TEMP L62 JAI503WPIINV/A
```

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     FILE 'STNGUIDE' ENTERED AT 12:04:41 ON 20 DEC 2006
                D SAVED

     FILE 'WPIX' ENTERED AT 12:05:16 ON 20 DEC 2006
L63           10 SEA ABB=ON  PLU=ON  L58 NOT (L17 OR L18 OR L19)
L64            9 SEA ABB=ON  PLU=ON  L63 AND L22
                D TRI 1-9

     FILE 'STNGUIDE' ENTERED AT 12:06:29 ON 20 DEC 2006

     FILE 'REGISTRY' ENTERED AT 12:07:20 ON 20 DEC 2006
                SELECT L7 1- CN
                D SELECT

     FILE 'STNGUIDE' ENTERED AT 12:08:01 ON 20 DEC 2006

     FILE 'MEDLINE' ENTERED AT 12:08:05 ON 20 DEC 2006
                E PYRIDAZIN/CT
L65             QUE ABB=ON  PLU=ON  PYRIDAZINES+PFT,OLD,NEW,NT/CT
                E THIOPHENE/CT
L66             QUE ABB=ON  PLU=ON  THIOPHENES+PFT,OLD,NEW,NT/CT
                E THIAZOLES/CT
L67             QUE ABB=ON  PLU=ON  THIAZOLES+PFT,OLD,NEW,NT/CT
L68           257 SEA ABB=ON  PLU=ON  L65 AND (L66 OR L67 OR L28)
                E PHOSPHODIESTERASE/CT
                E E148+ALL
L69             QUE ABB=ON  PLU=ON  "PHOSPHODIESTERASE INHIBITORS"+PFT,OLD,NEW,
                NT/CT
L70             QUE ABB=ON  PLU=ON  "PHOSPHODIESTERASES/ANTAGONISTS & INHIBITOR
                S"+PFT,OLD,NEW,NT/CT
L71            11 SEA ABB=ON  PLU=ON  L68 AND (L24 OR (L69 OR L70))
                SAVE TEMP L71 JAI503MED1B/A
                D TRI 5-10
L72             2 SEA ABB=ON  PLU=ON  L68 AND (L17 OR L18 OR L19)
                SAVE TEMP L72 JAI503MEDINV/A

     FILE 'EMBASE' ENTERED AT 12:12:28 ON 20 DEC 2006
                E PYRIDAZIN/CT
                E PYRIDAZINE/CT
L*** DEL        QUE "PYRIDAZINE DERIVATIVE"
L73             QUE ABB=ON  PLU=ON  "PYRIDAZINE DERIVATIVE"+PFT,OLD,NEW,NT/CT
                E PYRIDAZINONE/CT
L74             QUE ABB=ON  PLU=ON  "PYRIDAZINONE DERIVATIVE"+PFT,OLD,NEW,NT/CT

                E THIAZOLE/CT
                E THIAZOLE DERIVATIVE/CT

     FILE 'STNGUIDE' ENTERED AT 12:14:14 ON 20 DEC 2006

     FILE 'EMBASE' ENTERED AT 12:19:01 ON 20 DEC 2006
L75             QUE ABB=ON  PLU=ON  "THIAZOLE DERIVATIVE"+PFT,OLD,NEW,NT/CT
                E THIOPHENE/CT
                E THIOPHENE DERIV/CT
L76             QUE ABB=ON  PLU=ON  "THIOPHENE DERIVATIVE"+PFT,OLD,NEW,NT/CT
L77           217 SEA ABB=ON  PLU=ON  (L73 OR L74) AND ((L75 OR L76) OR L28)
                E PHOSPHODIESTERASE/CT
                E PHOSPHODIESTERASE INHIBITOR/CT
L78             QUE ABB=ON  PLU=ON  "PHOSPHODIESTERASE INHIBITOR"+PFT,OLD,NEW,N
                T/CT
L79           102 SEA ABB=ON  PLU=ON  L77 AND L78
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L80          67 SEA ABB=ON  PLU=ON  L79/MAJ
L81          59 SEA ABB=ON  PLU=ON  L80 AND L21
L82          41 SEA ABB=ON  PLU=ON  L81 AND (L75 OR L76)
                D TRI 30-35
L83          49 SEA ABB=ON  PLU=ON  L27(5A)L28
L84           0 SEA ABB=ON  PLU=ON  L83 AND L78
L85          14 SEA ABB=ON  PLU=ON  L77 AND L83
L86           0 SEA ABB=ON  PLU=ON  L83 AND L24
L87          14 SEA ABB=ON  PLU=ON  (L84 OR L85 OR L86)
                SAVE TEMP L87 JAI503EMBB/A
L88           3 SEA ABB=ON  PLU=ON  L77 AND (L17 OR L18 OR L19)
                SAVE TEMP L88 JAI503EMBINV/A

     FILE 'STNGUIDE' ENTERED AT 12:24:37 ON 20 DEC 2006
                D SAVED

     FILE 'BIOSIS, PASCAL, JICST-EPLUS, JAPIO, LIFESCI, BIOENG, BIOTECHNO,
     BIOTECHDS, DRUGU, DRUGB, VETU, VETB, SCISEARCH, CONFSCI, DISSABS' ENTERED
     AT 12:26:38 ON 20 DEC 2006
L89         348 SEA ABB=ON  PLU=ON  L27(5A) L28
L90           0 SEA ABB=ON  PLU=ON  L89 AND L24
L91         423 SEA ABB=ON  PLU=ON  L27(7A) L28
L92           1 SEA ABB=ON  PLU=ON  L91 AND L24
                D SCAN
                D TRI
                SAVE TEMP L92 JAI503MULB/A
L93           1 SEA ABB=ON  PLU=ON  L91 AND (L19 OR L20)
                SAVE TEMP L93 JAI503MULINV/A
                D SAVED

     FILE 'STNGUIDE' ENTERED AT 12:30:50 ON 20 DEC 2006

     FILE 'MARPAT' ENTERED AT 12:31:08 ON 20 DEC 2006
                D QUE L15
L94           3 SEA SSS SAM L13
                D QUE STAT
L95          57 SEA SSS FUL L13
                SAVE TEMP L95 JAI503MARP/A

     FILE 'LREGISTRY' ENTERED AT 12:32:07 ON 20 DEC 2006
                D QUE L7
L96             STR L9

     FILE 'MARPAT' ENTERED AT 12:35:04 ON 20 DEC 2006
L97           0 SEA SUB=L95 SSS SAM L96
                D QUE STAT
L98           2 SEA SUB=L95 SSS FUL L96
                SAVE TEMP L98 JAI503MARR/A
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 12:36:32 ON 20 DEC 2006
                D SAVED
                D QUE STAT L7
                D QUE NOS L8
                D L8 1-
                D QUE STAT L15
                D QUE NOS L16
                D L16 1-
                D QUE L35
                D QUE NOS L43
```

```
             D QUE NOS L46
             D QUE NOS L48
             D QUE STAT L49
             D QUE L51
             D QUE STAT L53
             D QUE STAT L55
             D QUE NOS L58
             D QUE STAT L95
             D QUE STAT L98
             D QUE L71
             D QUE L87
             D QUE L92

    FILE 'HCAPLUS, USPATFULL, TOXCENTER, CASREACT, BABS, CHEMINFORMRX, WPIX,
    MARPAT, MEDLINE, EMBASE, DRUGU' ENTERED AT 12:42:22 ON 20 DEC 2006
L99          69 DUP REM L35 L43 L46 L48 L51 L53 L58 L98 L71 L87...  (21 DUPLI
                    ANSWERS '1-32' FROM FILE HCAPLUS
                    ANSWERS '33-34' FROM FILE USPATFULL
                    ANSWER '35' FROM FILE TOXCENTER
                    ANSWERS '36-37' FROM FILE CHEMINFORMRX
                    ANSWERS '38-42' FROM FILE WPIX
                    ANSWER '43' FROM FILE MARPAT
                    ANSWERS '44-54' FROM FILE MEDLINE
                    ANSWERS '55-68' FROM FILE EMBASE
                    ANSWER '69' FROM FILE DRUGU

    FILE 'STNGUIDE' ENTERED AT 12:42:35 ON 20 DEC 2006

    FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX, WPIX, MEDLINE, EMBASE,
    DRUGU, MARPAT' ENTERED AT 12:43:22 ON 20 DEC 2006
             D IBIB ED AB HITIND RETABLE HITSTR

    FILE 'STNGUIDE' ENTERED AT 12:43:30 ON 20 DEC 2006

    FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX, WPIX, MEDLINE, EMBASE,
    DRUGU, MARPAT' ENTERED AT 12:44:12 ON 20 DEC 2006
             D IBIB ED AB HITIND RETABLE HITSTR 2-32

    FILE 'STNGUIDE' ENTERED AT 12:45:14 ON 20 DEC 2006

    FILE 'BEILSTEIN' ENTERED AT 12:45:58 ON 20 DEC 2006
             D L50 IDE

    FILE 'STNGUIDE' ENTERED AT 12:45:59 ON 20 DEC 2006

    FILE 'BEILSTEIN' ENTERED AT 12:46:08 ON 20 DEC 2006
             D L50 RX

    FILE 'STNGUIDE' ENTERED AT 12:46:10 ON 20 DEC 2006

    FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX, WPIX, MEDLINE, EMBASE,
    DRUGU, MARPAT' ENTERED AT 12:46:26 ON 20 DEC 2006
             D IBIB AB HITSTR 33-34

    FILE 'STNGUIDE' ENTERED AT 12:46:28 ON 20 DEC 2006

    FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX, WPIX, MEDLINE, EMBASE,
    DRUGU, MARPAT' ENTERED AT 12:46:42 ON 20 DEC 2006
             D IBIB ED AB HITIND 35
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FILE 'STNGUIDE' ENTERED AT 12:46:43 ON 20 DEC 2006

FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX, WPIX, MEDLINE, EMBASE,
DRUGU, MARPAT' ENTERED AT 12:46:58 ON 20 DEC 2006
           D IBIB ED AB HIT 36

FILE 'STNGUIDE' ENTERED AT 12:47:05 ON 20 DEC 2006

FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX, WPIX, MEDLINE, EMBASE,
DRUGU, MARPAT' ENTERED AT 12:47:16 ON 20 DEC 2006
           D BIB AB HIT 37

FILE 'STNGUIDE' ENTERED AT 12:47:18 ON 20 DEC 2006

FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX, WPIX, MEDLINE, EMBASE,
DRUGU, MARPAT' ENTERED AT 12:47:36 ON 20 DEC 2006
           D IALL ABEQ TECH ABEX HITSTR 38-42

FILE 'STNGUIDE' ENTERED AT 12:47:45 ON 20 DEC 2006

FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX, WPIX, MEDLINE, EMBASE,
DRUGU, MARPAT' ENTERED AT 12:48:15 ON 20 DEC 2006
           D IBIB AB FHIT 43

FILE 'STNGUIDE' ENTERED AT 12:48:16 ON 20 DEC 2006

FILE 'HCAPLUS, USPATFULL, TOXCENTER, CHEMINFORMRX, WPIX, MEDLINE, EMBASE,
DRUGU, MARPAT' ENTERED AT 12:49:15 ON 20 DEC 2006
           D IBIB ED AB IND 44-69

FILE 'STNGUIDE' ENTERED AT 12:49:17 ON 20 DEC 2006
           D QUE NOS L36
           D QUE NOS L47
           D QUE NOS L62
           D QUE L72
           D QUE L88
           D QUE L93

FILE 'HCAPLUS, TOXCENTER, WPIX, MEDLINE, EMBASE, BIOSIS' ENTERED AT
12:51:07 ON 20 DEC 2006
L100         9 DUP REM L36 L47 L62 L72 L88 L93 (2 DUPLICATES REMOVED)
                 ANSWERS '1-3' FROM FILE HCAPLUS
                 ANSWERS '4-5' FROM FILE MEDLINE
                 ANSWERS '6-8' FROM FILE EMBASE
                 ANSWER '9' FROM FILE BIOSIS

FILE 'STNGUIDE' ENTERED AT 12:51:14 ON 20 DEC 2006

FILE 'HCAPLUS, MEDLINE, EMBASE, BIOSIS' ENTERED AT 12:51:22 ON 20 DEC 2006
           D IBIB ED AB 1-9

FILE 'STNGUIDE' ENTERED AT 12:51:23 ON 20 DEC 2006

FILE 'STNGUIDE' ENTERED AT 12:51:32 ON 20 DEC 2006


FILE HOME

FILE ZCAPLUS
```

FILE COVERS 1907 - 20 Dec 2006 VOL 145 ISS 26
FILE LAST UPDATED: 19 Dec 2006 (20061219/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE HCAPLUS

FILE COVERS 1907 - 20 Dec 2006 VOL 145 ISS 26
FILE LAST UPDATED: 19 Dec 2006 (20061219/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE STNGUIDE
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Dec 19, 2006 (20061219/UP).

FILE WPIX
FILE LAST UPDATED: 18 DEC 2006 <20061218/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE: 200681 <200681/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> YOU ARE IN THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX <<<

FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf

>>> FOR DETAILS ON THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX
PLEASE SEE
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 DEC 2006 HIGHEST RN 916029-54-4
DICTIONARY FILE UPDATES: 19 DEC 2006 HIGHEST RN 916029-54-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE LREGISTRY
LREGISTRY IS A STATIC LEARNING FILE

NEW CAS INFORMATION USE POLICIES, ENTER HELP USAGETERMS FOR DETAILS.

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 19 Dec 2006 (20061219/PD)
FILE LAST UPDATED: 19 Dec 2006 (20061219/ED)
HIGHEST GRANTED PATENT NUMBER: US7152245
HIGHEST APPLICATION PUBLICATION NUMBER: US2006282930
CA INDEXING IS CURRENT THROUGH 19 Dec 2006 (20061219/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 19 Dec 2006 (20061219/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2006

FILE USPAT2

FILE COVERS 2001 TO PUBLICATION DATE: 19 Dec 2006 (20061219/PD)
FILE LAST UPDATED: 19 Dec 2006 (20061219/ED)
HIGHEST GRANTED PATENT NUMBER: US2006182892
HIGHEST APPLICATION PUBLICATION NUMBER: US2006282212
CA INDEXING IS CURRENT THROUGH 19 Dec 2006 (20061219/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 19 Dec 2006 (20061219/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2006

FILE TOXCENTER

FILE COVERS 1907 TO 19 Dec 2006 (20061219/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

The MEDLINE file segment has been updated with 2007 MeSH terms.and See HELP RLOAD for details.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2007 vocabulary.

FILE CASREACT

FILE CONTENT:1840 - 17 Dec 2006 VOL 145 ISS 25

New CAS Information Use Policies, enter HELP USAGETERMS for details.

```
**********************************************************
*                                                        *
*     CASREACT now has more than 10 million reactions    *
*                                                        *
**********************************************************
```

Some CASREACT records are derived from the ZIC/VINITI database (1974-1991) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BEILSTEIN
FILE LAST UPDATED ON JUNE 16, 2006

FILE COVERS 1771 TO 2006.
FILE CONTAINS 9,606,495 SUBSTANCES

>>>PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For mo detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

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************************************************************
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST.      *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS.              *
* FOR PRICE INFORMATION SEE HELP COST                      *
************************************************************
```

NEW

*** PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE SEARCHED, SELECTED AND TRANSFERRED.**
*** NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES, ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A COMPOUND AT A GLANCE.**

FILE BABS
FILE LAST UPDATED: 25 SEP 2006 <20060925/UP>
FILE COVERS 1980 TO DATE.

FILE CHEMINFORMRX
FILE LAST UPDATED: 5 DEC 2006 <20061205/UP>

>>> CAS Registry Numbers are available for
substances prior to 1995 <<<

FILE MEDLINE
FILE LAST UPDATED: 19 Dec 2006 (20061219/UP). FILE COVERS 1950 TO DATE.

All regular MEDLINE updates from November 15 to December 16 have been added to MEDLINE, along with 2007 Medical Subject Headings (MeSH(R)) and 2007 tree numbers.

The annual reload will be available in early 2007.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE EMBASE
FILE COVERS 1974 TO 20 Dec 2006 (20061220/ED)

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 14 December 2006 (20061214/ED)

FILE PASCAL
FILE LAST UPDATED: 18 DEC 2006 <20061218/UP>
FILE COVERS 1977 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE
IN THE BASIC INDEX (/BI) FIELD <<<

FILE JICST-EPLUS
FILE COVERS 1985 TO 18 DEC 2006 (20061218/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE JAPIO
FILE LAST UPDATED: 12 DEC 2006 <20061212/UP>

FILE COVERS APRIL 1973 TO AUGUST 31, 2006

>>> GRAPHIC IMAGES AVAILABLE <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN FILE JAPIO.
SEE HELP CHANGE
AND
http://www.stn-international.de/stndatabases/details/ipc_reform.html <<<

FILE LIFESCI
FILE COVERS 1978 TO 10 Nov 2006 (20061110/ED)

FILE BIOENG
FILE LAST UPDATED: 20 NOV 2006 <20061120/UP>
FILE COVERS 1982 TO DATE

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
THE BASIC INDEX <<<

FILE BIOTECHNO
FILE LAST UPDATED: 7 JAN 2004 <20040107/UP>
FILE COVERS 1980 TO 2003.

>>> BIOTECHNO IS NO LONGER BEING UPDATED AS OF 2004 <<<

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
/CT AND BASIC INDEX <<<

FILE BIOTECHDS
FILE LAST UPDATED: 13 DEC 2006 <20061213/UP>
FILE COVERS 1982 TO DATE

>>> USE OF THIS FILE IS LIMITED TO BIOTECH SUBSCRIBERS <<<

FILE DRUGU
FILE LAST UPDATED: 19 DEC 2006 <20061219/UP>
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<
>>> THESAURUS AVAILABLE IN /CT <<<

FILE DRUGB
>>> FILE COVERS 1964 TO 1982 - CLOSED FILE <<<

FILE VETU
FILE LAST UPDATED: 02 JAN 2002 <20020102/UP>
FILE COVERS 1983-2001

FILE VETB
FILE LAST UPDATED: 25 SEP 94 <940925/UP>
FILE COVERS 1968-1982

FILE SCISEARCH

FILE COVERS 1974 TO 14 Dec 2006 (20061214/ED)

SCISEARCH has been reloaded, see HELP RLOAD for details.

FILE CONFSCI

FILE COVERS 1973 TO 14 Nov 2006 (20061114/ED)

CSA has resumed updates, see NEWS FILE

FILE DISSABS
FILE COVERS 1861 TO 27 NOV 2006 (20061127/ED)

FILE MARPAT
FILE CONTENT: 1961-PRESENT VOL 145 ISS 25 (20061215/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES (COVERAGE TO THESE DATES IS NOT COMPLETE):

US	20060247444	02 NOV 2006
DE	102005020105	26 OCT 2006
EP	1717297	02 NOV 2006
JP	2006302757	02 NOV 2006
WO	2006116773	02 NOV 2006
GB	2425654	01 NOV 2006
FR	2884821	27 OCT 2006
RU	2286328	27 OCT 2006
CA	2545188	28 OCT 2006

Expanded G-group definition display now available.

=>